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* * * * * Welcome to STN International * * * * *

NEWS	1		Web Page for STN Seminar Schedule - N. America
NEWS	2	DEC 01	ChemPort single article sales feature unavailable
NEWS	3	FEB 02	Simultaneous left and right truncation (SLART) added for CERAB, COMPUAB, ELCOM, and SOLIDSTATE
NEWS	4	FEB 02	GENBANK enhanced with SET PLURALS and SET SPELLING
NEWS	5	FEB 06	Patent sequence location (PSL) data added to USGENE
NEWS	6	FEB 10	COMPENDEX reloaded and enhanced
NEWS	7	FEB 11	WTEXTILES reloaded and enhanced
NEWS	8	FEB 19	New patent-examiner citations in 300,000 CA/CAPLUS patent records provide insights into related prior art
NEWS	9	FEB 19	Increase the precision of your patent queries -- use terms from the IPC Thesaurus, Version 2009.01
NEWS	10	FEB 23	Several formats for image display and print options discontinued in USPATFULL and USPAT2
NEWS	11	FEB 23	MEDLINE now offers more precise author group fields and 2009 MeSH terms
NEWS	12	FEB 23	TOXCENTER updates mirror those of MEDLINE - more precise author group fields and 2009 MeSH terms
NEWS	13	FEB 23	Three million new patent records blast AEROSPACE into STN patent clusters
NEWS	14	FEB 25	USGENE enhanced with patent family and legal status display data from INPADOCDB
NEWS	15	MAR 06	INPADOCDB and INPAFAMDB enhanced with new display formats
NEWS	16	MAR 11	EPFULL backfile enhanced with additional full-text applications and grants
NEWS	17	MAR 11	ESBIOBASE reloaded and enhanced
NEWS	18	MAR 20	CAS databases on STN enhanced with new super role for nanomaterial substances
NEWS	19	MAR 23	CA/CAPLUS enhanced with more than 250,000 patent equivalents from China
NEWS	20	MAR 30	IMSPATENTS reloaded and enhanced
NEWS	21	APR 03	CAS coverage of exemplified prophetic substances enhanced
NEWS	22	APR 07	STN is raising the limits on saved answers
NEWS	23	APR 24	CA/CAPLUS now has more comprehensive patent assignee information
NEWS	24	APR 26	USPATFULL and USPAT2 enhanced with patent assignment/reassignment information
NEWS	25	APR 28	CAS patent authority coverage expanded
NEWS	26	APR 28	ENCOMPLIT/ENCOMPLIT2 search fields enhanced
NEWS	27	APR 28	Limits doubled for structure searching in CAS

REGISTRY

NEWS EXPRESS JUNE 27 08 CURRENT WINDOWS VERSION IS V8.3,
AND CURRENT DISCOVER FILE IS DATED 23 JUNE 2008.

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* * * * * STN Columbus * * * * *

FILE 'HOME' ENTERED AT 14:33:15 ON 06 MAY 2009

=> fil casreact

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.22	0.22

FILE 'CASREACT' ENTERED AT 14:33:53 ON 06 MAY 2009
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FILE CONTENT:1840 - 3 May 2009 VOL 150 ISS 19

New CAS Information Use Policies, enter HELP USAGETERMS for details.

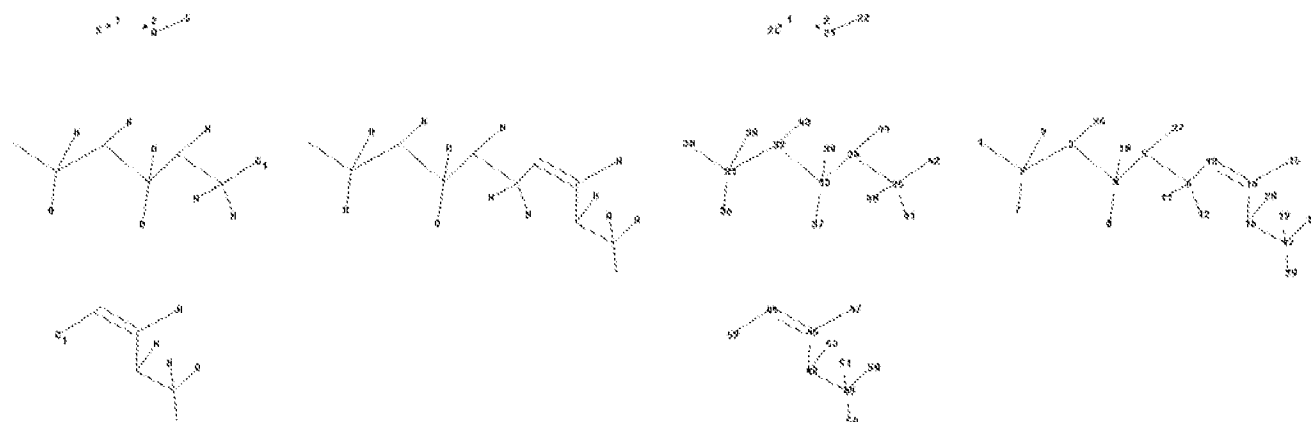
* CASREACT now has more than 16.5 million reactions *
* *

CASREACT contains reactions from CAS and from: ZIC/VINITI database
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This file contains CAS Registry Numbers for easy and accurate substance
identification.

=>

Uploading C:\Program Files\STNEXP\Queries\10575136.str



chain nodes :

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 26
27 28 29 30 31 32 33 34 35 37 38 39 40 41 42 43 44 45 46 47 48
49 50 51 52
53 54

ring/chain nodes :

36

chain bonds :

1-2 2-3 2-7 2-9 3-4 3-26 4-5 4-8 4-10 5-6 5-27 6-11 6-12 6-13 13-14
14-15 14-16 16-17 16-28 17-18 17-19 17-29 21-22 30-31 31-32 31-36 31-38
32-33 32-43
33-34 33-37 33-39 34-35 34-44 35-40 35-41 35-42 45-46 45-52 46-47 46-48
48-49 48-53
49-50 49-51 49-54

exact/norm bonds :

2-7 4-8 17-18 21-22 31-36 33-37 35-42 45-52 49-50

exact bonds :

1-2 2-3 2-9 3-4 3-26 4-5 4-10 5-6 5-27 6-11 6-12 6-13 13-14 14-15 14-16
16-17 16-28 17-19 17-29 30-31 31-32 31-38 32-33 32-43 33-34 33-39 34-35
34-44 35-40
35-41 45-46 46-47 46-48 48-49 48-53 49-51 49-54

G1:[*1],[*2]

Match level :

1:CLASS 2:CLASS 3:CLASS 4:CLASS 5:CLASS 6:CLASS 7:CLASS 8:CLASS 9:CLASS
10:CLASS 11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS
18:CLASS 19:CLASS
20:CLASS 21:CLASS 22:CLASS 26:CLASS 27:CLASS 28:CLASS 29:CLASS 30:CLASS
31:CLASS 32:CLASS
33:CLASS 34:CLASS 35:CLASS 36:CLASS 37:CLASS 38:CLASS 39:CLASS 40:CLASS
41:CLASS 42:CLASS
43:CLASS 44:CLASS 45:CLASS 46:CLASS 47:CLASS 48:CLASS 49:CLASS 50:CLASS
51:CLASS 52:CLASS
53:CLASS 54:CLASS

fragments assigned product role:

containing 1
fragments assigned reactant/reagent role:
containing 30
containing 45
node mappings:
6:35 13:45

L1 STRUCTURE UPLOADED

=> s sss l1

SAMPLE SEARCH INITIATED 14:34:24 FILE 'CASREACT'
SCREENING COMPLETE - 835 REACTIONS TO VERIFY FROM 29 DOCUMENTS

100.0% DONE 835 VERIFIED 0 HIT RXNS 0 DOCS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED VERIFICATIONS: 14968 TO 18432
PROJECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1 (0 REACTIONS)

=> d l1

L1 HAS NO ANSWERS
L1 STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.

=> s sss l1 full

FULL SEARCH INITIATED 14:39:59 FILE 'CASREACT'
SCREENING COMPLETE - 21014 REACTIONS TO VERIFY FROM 671 DOCUMENTS

100.0% DONE 21014 VERIFIED 182 HIT RXNS (6 INCOMP) 9 DOCS
SEARCH TIME: 00.00.05

L3 9 SEA SSS FUL L1 (182 REACTIONS)

=> d scan

L3 9 ANSWERS CASREACT COPYRIGHT 2009 ACS on STN

TI Total Synthesis of (+)-Discodermolide

RX(5) OF 7 - REACTION DIAGRAM NOT AVAILABLE

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L3 9 ANSWERS CASREACT COPYRIGHT 2009 ACS on STN

TI Preparation of discodermolide analogs for use in pharmaceutical
compositions as antiproliferative agents

RX(12) OF 136 - REACTION DIAGRAM NOT AVAILABLE

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> d 13 1

L3 ANSWER 1 OF 9 CASREACT COPYRIGHT 2009 ACS on STN

RX(33) OF 320 - REACTION DIAGRAM NOT AVAILABLE

=> d 13 occ 1-9

L3 ANSWER 1 OF 9 CASREACT COPYRIGHT 2009 ACS on STN

NUMBER OF HIT REACTIONS	4
NUMBER OF REACTIONS IN PATH	1
NUMBER OF REACTIONS IN SPATH	2
FIELD	COUNT
RX(33)	3
RX(69)	3
RX(132)	3
RX(136)	3

L3 ANSWER 2 OF 9 CASREACT COPYRIGHT 2009 ACS on STN

NUMBER OF HIT REACTIONS	15
NUMBER OF REACTIONS IN PATH	3
NUMBER OF REACTIONS IN SPATH	4
FIELD	COUNT
RX(12)	3
RX(42)	3
RX(69)	3
RX(71)	3
RX(98)	3
RX(100)	3
RX(103)	3
RX(113)	3
RX(114)	3
RX(115)	3
RX(130)	3
RX(131)	3
RX(132)	3
RX(135)	3
RX(136)	3

L3 ANSWER 3 OF 9 CASREACT COPYRIGHT 2009 ACS on STN

NUMBER OF HIT REACTIONS	17
NUMBER OF REACTIONS IN PATH	2
NUMBER OF REACTIONS IN SPATH	3
FIELD	COUNT
RX(1)	3
RX(18)	3
RX(31)	3
RX(41)	3
RX(55)	3
RX(78)	3
RX(81)	3
RX(88)	3
RX(89)	3

RX(99)	3	(INCOMPLETE)
RX(100)	3	
RX(106)	3	(INCOMPLETE)
RX(111)	3	(INCOMPLETE)
RX(115)	3	
RX(117)	3	(INCOMPLETE)
RX(118)	3	(INCOMPLETE)
RX(119)	3	(INCOMPLETE)

L3 ANSWER 4 OF 9 CASREACT COPYRIGHT 2009 ACS on STN

NUMBER OF HIT REACTIONS	30
NUMBER OF REACTIONS IN PATH	2
NUMBER OF REACTIONS IN SPATH	4
FIELD	COUNT
RX(20)	3
RX(27)	3
RX(55)	3
RX(62)	3
RX(104)	3
RX(107)	3
RX(116)	3
RX(119)	3
RX(151)	3
RX(152)	3
RX(153)	3
RX(154)	3
RX(155)	3
RX(156)	3
RX(164)	3
RX(165)	3
RX(174)	3
RX(190)	3
RX(201)	3
RX(209)	3
RX(217)	3
RX(218)	3
RX(219)	3
RX(220)	3
RX(236)	3
RX(237)	3
RX(238)	3
RX(248)	3
RX(254)	3
RX(258)	3
NUMBER OF HIT REACTIONS	30
NUMBER OF REACTIONS IN PATH	2
NUMBER OF REACTIONS IN SPATH	4

L3 ANSWER 5 OF 9 CASREACT COPYRIGHT 2009 ACS on STN

NUMBER OF HIT REACTIONS	36
NUMBER OF REACTIONS IN PATH	4
NUMBER OF REACTIONS IN SPATH	6
FIELD	COUNT
RX(13)	3
RX(17)	3
RX(21)	3
RX(39)	3
RX(43)	3

RX(46)	3
RX(47)	3
RX(73)	3
RX(79)	3
RX(80)	3
RX(81)	3
RX(82)	3
RX(84)	3
RX(85)	3
RX(86)	3
RX(87)	3
RX(88)	3
RX(89)	3
RX(91)	3
RX(93)	3
RX(136)	3
RX(137)	3
RX(138)	3
RX(139)	3
RX(140)	3
RX(141)	3
RX(142)	3
RX(143)	3
RX(144)	3
RX(145)	3
RX(146)	3
RX(147)	3
RX(148)	3
RX(149)	3
RX(150)	3
RX(151)	3
NUMBER OF HIT REACTIONS	36
NUMBER OF REACTIONS IN PATH	4
NUMBER OF REACTIONS IN SPATH	6

L3 ANSWER 6 OF 9 CASREACT COPYRIGHT 2009 ACS on STN

NUMBER OF HIT REACTIONS	21
NUMBER OF REACTIONS IN PATH	6
NUMBER OF REACTIONS IN SPATH	7
FIELD	COUNT
RX(35)	3
RX(39)	3
RX(41)	3
RX(75)	3
RX(81)	3
RX(150)	3
RX(151)	3
RX(154)	3
RX(157)	3
RX(313)	3
RX(314)	3
RX(382)	3
RX(398)	3
RX(503)	3
RX(504)	3
RX(507)	3
RX(508)	3
RX(529)	3
RX(530)	3

RX(567)	3
RX(568)	3
NUMBER OF HIT REACTIONS	21
NUMBER OF REACTIONS IN PATH	6
NUMBER OF REACTIONS IN SPATH	7

L3	ANSWER 7 OF 9	CASREACT	COPYRIGHT 2009 ACS on STN
NUMBER OF HIT REACTIONS	2		
NUMBER OF REACTIONS IN PATH	1		
NUMBER OF REACTIONS IN SPATH	2		
FIELD	COUNT		
RX(17)	3		
RX(33)	3		

L3	ANSWER 8 OF 9	CASREACT	COPYRIGHT 2009 ACS on STN
NUMBER OF HIT REACTIONS	56		
NUMBER OF REACTIONS IN PATH	2		
NUMBER OF REACTIONS IN SPATH	2		
FIELD	COUNT		
RX(11)	3		
RX(44)	3		
RX(61)	3		
RX(87)	3		
RX(89)	3		
RX(115)	3		
RX(116)	3		
RX(121)	3		
RX(122)	3		
RX(123)	3		
RX(124)	3		
RX(125)	3		
RX(127)	3		
RX(175)	3		
RX(178)	3		
RX(179)	3		
RX(180)	3		
RX(181)	3		
RX(222)	3		
RX(226)	3		
RX(227)	3		
RX(230)	3		
RX(231)	3		
RX(232)	3		
RX(238)	3		
RX(239)	3		
RX(240)	3		
RX(241)	3		
RX(242)	3		
RX(243)	3		
RX(244)	3		
RX(245)	3		
RX(246)	3		
RX(247)	3		
RX(248)	3		
RX(249)	3		
RX(250)	3		
RX(252)	3		
RX(304)	3		

RX(306)	3
RX(308)	3
RX(310)	3
RX(312)	3
RX(314)	3
RX(316)	3
RX(318)	3
RX(320)	3
RX(322)	3
RX(324)	3
RX(326)	3
RX(348)	3
RX(349)	3
RX(350)	3
RX(351)	3
RX(352)	3
RX(353)	3
NUMBER OF HIT REACTIONS	56
NUMBER OF REACTIONS IN PATH	2
NUMBER OF REACTIONS IN SPATH	2

L3 ANSWER 9 OF 9 CASREACT COPYRIGHT 2009 ACS on STN

NUMBER OF HIT REACTIONS	1
NUMBER OF REACTIONS IN PATH	1
NUMBER OF REACTIONS IN SPATH	1
FIELD	COUNT
RX(5)	3

=> d ibib abs hit 13 1-9

L3 ANSWER 1 OF 9 CASREACT COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 147:52745 CASREACT Full-text

TITLE: α -Oxygenated crotyltitanium and dyotropic rearrangement in the total synthesis of discodermolide

AUTHOR(S): de Lemos, Elsa; Poree, Francois-Hugues; Commercon, Alain; Betzer, Jean-Francois; Pancrazi, Ange; Ardisson, Janick

CORPORATE SOURCE: CNRS UMR 8123, Universite de Cergy-Pontoise, Cergy Pontoise, 95031, Fr.

SOURCE: Angewandte Chemie, International Edition (2007), 46(11), 1917-1921
CODEN: ACIEF5; ISSN: 1433-7851

PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA

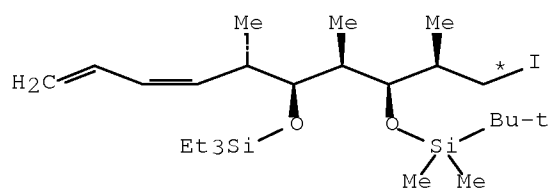
DOCUMENT TYPE: Journal

LANGUAGE: English

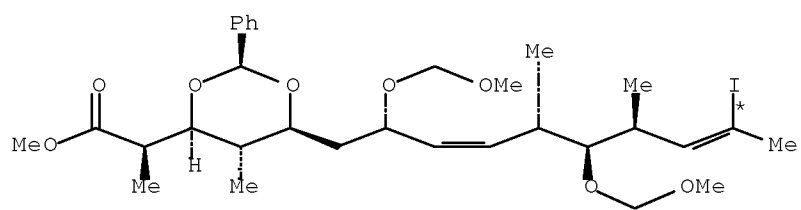
AB The total synthesis of discodermolide relies on the elaboration of syn-anti stereotriads linked to a Z-O-enecarbamate group, its direct transformation into the terminal Z diene, and stereocontrolled generation of the trisubstituted Z double bond by a dyotropic rearrangement. The synthesis was achieved in 21 steps with 1.6% overall yield.

REFERENCE COUNT: 88 THERE ARE 88 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(33) OF 320 ...BZ + CQ ==> CU...

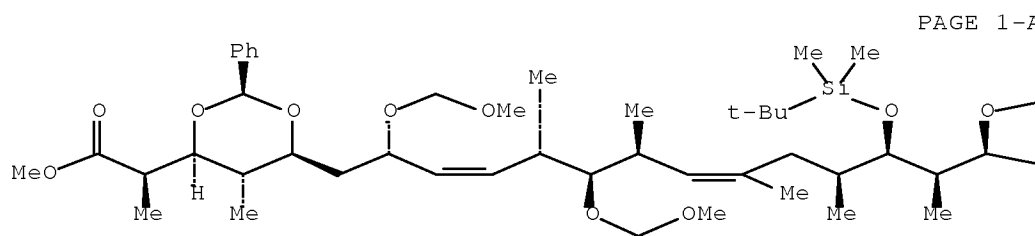


BZ



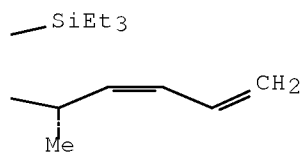
CQ

(33) →



PAGE 1-A

PAGE 1-B



CU
YIELD 60%

RX(33) RCT BZ 649755-91-9

STAGE(1)

RGT O 594-19-4 t-BuLi
 SOL 75-65-0 t-BuOH
 CON SUBSTAGE(1) -80 deg C
 SUBSTAGE(2) 2 minutes, -80 deg C

STAGE(2)

RGT CV 280-64-8 9-BBN
 SOL 109-99-9 THF
 CON SUBSTAGE(1) 10 minutes, -80 deg C
 SUBSTAGE(2) 75 minutes, -80 deg C -> room temperature

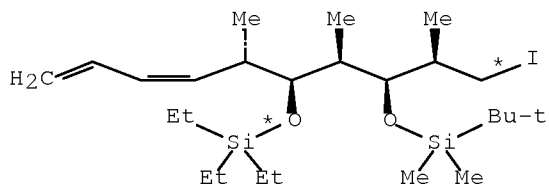
STAGE(3)

RCT CQ 939795-51-4
 RGT CW 534-17-8 Cs2CO3
 SOL 68-12-2 DMF
 CON 16 hours, room temperature

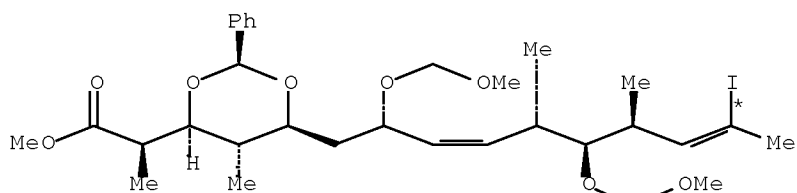
PRO CU 939795-52-5

RX(69) OF 320 COMPOSED OF RX(33), RX(34)

RX(69) BZ + CQ ==> CX

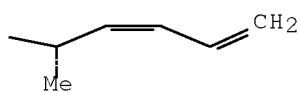
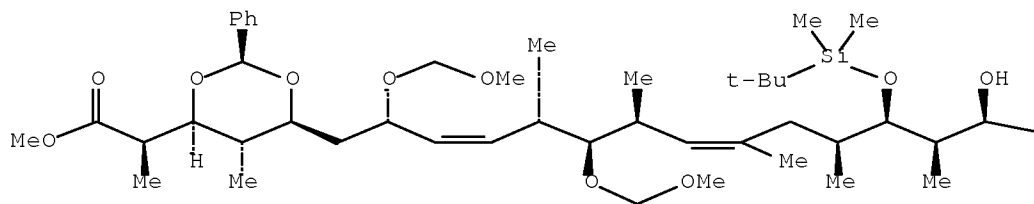


BZ



CQ

2
 STEPS
 →



CX
YIELD 77%

RX(33) RCT BZ 649755-91-9

STAGE(1)

RGT O 594-19-4 t-BuLi

SOL 75-65-0 t-BuOH

CON SUBSTAGE(1) -80 deg C

SUBSTAGE(2) 2 minutes, -80 deg C

STAGE(2)

RGT CV 280-64-8 9-BBN

SOL 109-99-9 THF

CON SUBSTAGE(1) 10 minutes, -80 deg C

SUBSTAGE(2) 75 minutes, -80 deg C -> room temperature

STAGE(3)

RCT CQ 939795-51-4

RGT CW 534-17-8 Cs2CO3

SOL 68-12-2 DMF

CON 16 hours, room temperature

PRO CU 939795-52-5

RX(34) RCT CU 939795-52-5

RGT I 104-15-4 TsOH

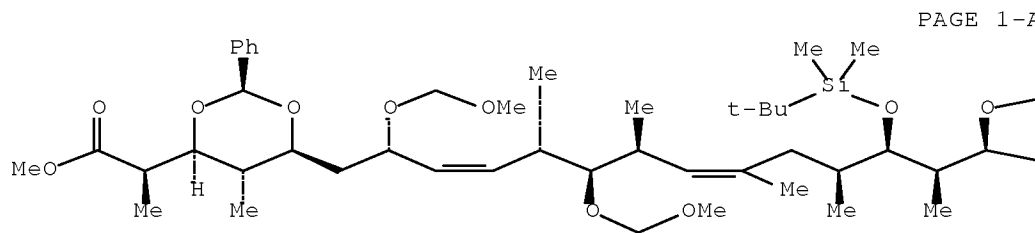
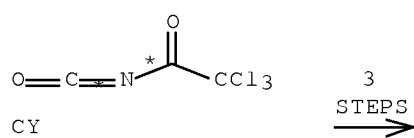
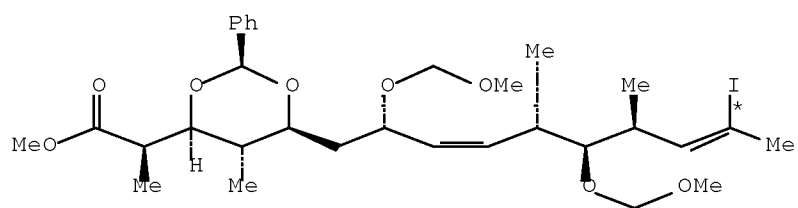
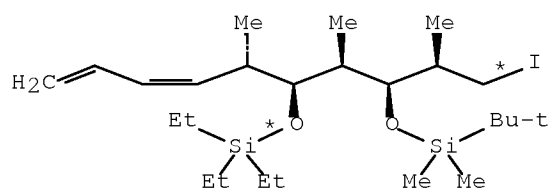
PRO CX 939795-64-9

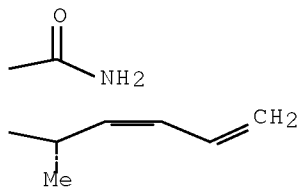
SOL 67-56-1 MeOH

CON 1 hour, 0 deg C

RX(132) OF 320 COMPOSED OF RX(33), RX(34), RX(35)

RX(132) BZ + CQ + CY ==> CZ





CZ
YIELD 64%

RX(33) RCT BZ 649755-91-9

STAGE(1)

RGT O 594-19-4 t-BuLi

SOL 75-65-0 t-BuOH

CON SUBSTAGE(1) -80 deg C

SUBSTAGE(2) 2 minutes, -80 deg C

STAGE(2)

RGT CV 280-64-8 9-BBN

SOL 109-99-9 THF

CON SUBSTAGE(1) 10 minutes, -80 deg C

SUBSTAGE(2) 75 minutes, -80 deg C -> room temperature

STAGE(3)

RCT CQ 939795-51-4

RGT CW 534-17-8 Cs2CO3

SOL 68-12-2 DMF

CON 16 hours, room temperature

PRO CU 939795-52-5

RX(34) RCT CU 939795-52-5
RGT I 104-15-4 TsOH
PRO CX 939795-64-9
SOL 67-56-1 MeOH
CON 1 hour, 0 deg C

RX(35) RCT CX 939795-64-9, CY 3019-71-4

STAGE(1)

SOL 75-09-2 CH2Cl2

CON 15 minutes, room temperature

STAGE(2)

RGT DA 584-08-7 K2CO3

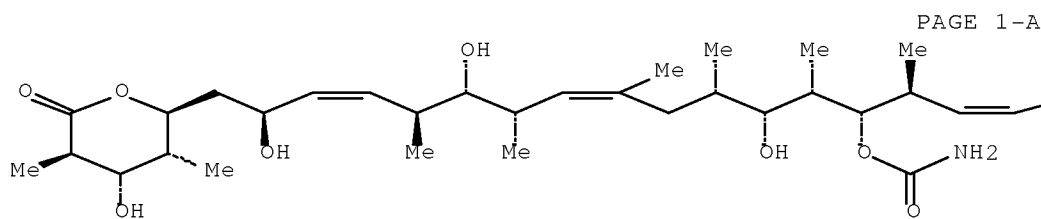
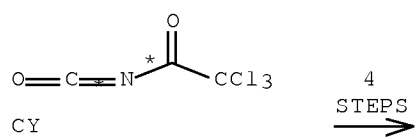
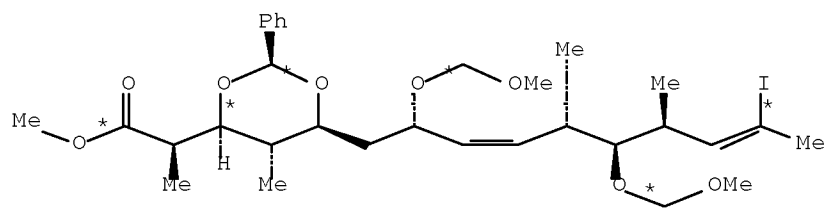
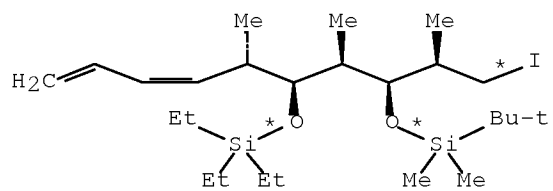
SOL 67-56-1 MeOH

CON 1.5 hours, room temperature

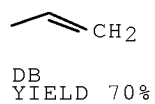
PRO CZ 939795-65-0

RX(136) OF 320 COMPOSED OF RX(33), RX(34), RX(35), RX(36)

RX(136) BZ + CQ + CY ==> DB



PAGE 1-B



RX(33) RCT BZ 649755-91-9

STAGE(1)

RGT O 594-19-4 t-BuLi

SOL 75-65-0 t-BuOH

CON SUBSTAGE(1) -80 deg C

SUBSTAGE(2) 2 minutes, -80 deg C

STAGE(2)

RGT CV 280-64-8 9-BBN

SOL 109-99-9 THF

CON SUBSTAGE(1) 10 minutes, -80 deg C

SUBSTAGE(2) 75 minutes, -80 deg C -> room temperature

STAGE(3)

RCT CQ 939795-51-4

RGT CW 534-17-8 Cs2CO3

SOL 68-12-2 DMF

CON 16 hours, room temperature

PRO CU 939795-52-5

RX(34) RCT CU 939795-52-5

RGT I 104-15-4 TsOH

PRO CX 939795-64-9

SOL 67-56-1 MeOH

CON 1 hour, 0 deg C

RX(35) RCT CX 939795-64-9, CY 3019-71-4

STAGE(1)

SOL 75-09-2 CH2Cl2

CON 15 minutes, room temperature

STAGE(2)

RGT DA 584-08-7 K2CO3

SOL 67-56-1 MeOH

CON 1.5 hours, room temperature

PRO CZ 939795-65-0

RX(36) RCT CZ 939795-65-0

RGT DC 7647-01-0 HCl

PRO DB 127943-53-7

SOL 109-99-9 THF

CON 72 hours, room temperature

L3 ANSWER 2 OF 9 CASREACT COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 144:467954 CASREACT Full-text

TITLE: Preparation of discodermolide analogs for use in pharmaceutical compositions as antiproliferative agents

INVENTOR(S): Sundermann, Kurt F.; Shaw, Simon James; Santi, Daniel V.

PATENT ASSIGNEE(S): Kosan Biosciences Incorporated, USA

SOURCE: U.S. Pat. Appl. Publ., 27 pp.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

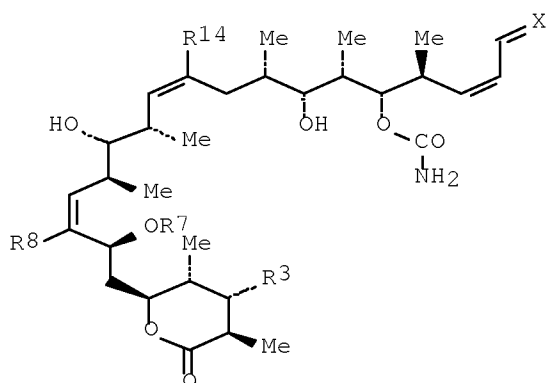
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20060106094	A1	20060518	US 2005-261686	20051028
US 7214708	B2	20070508		
WO 2006055472	A2	20060526	WO 2005-US41126	20051110
WO 2006055472	A3	20070215		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.:	US 2004-629401P	20041118
	US 2004-629518P	20041118
	US 2004-629519P	20041118
	US 2004-629520P	20041118
	US 2005-261686	20051028

OTHER SOURCE(S): MARPAT 144:467954
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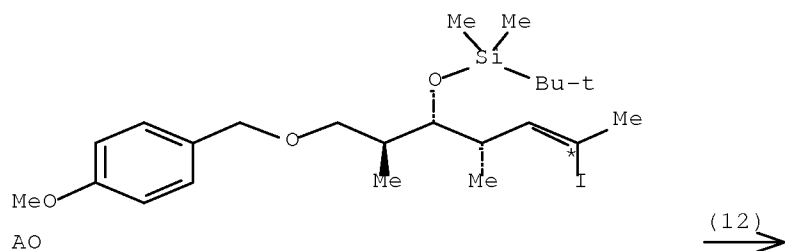
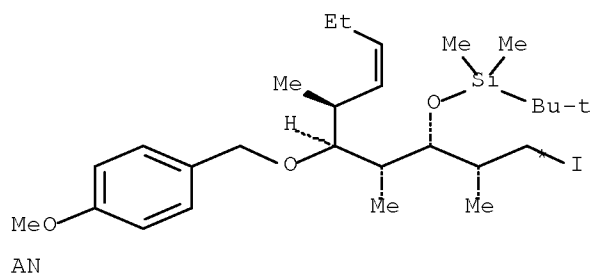


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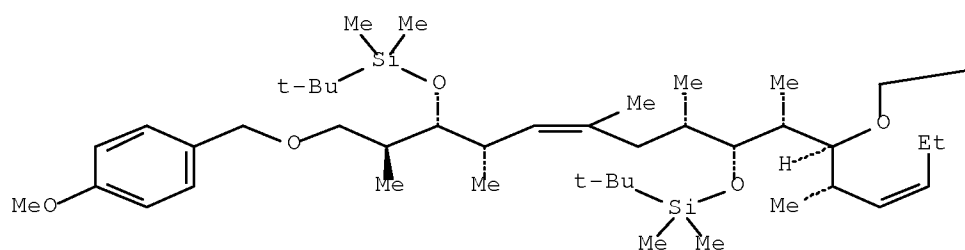
AB Discodermolide analogs, such as I [R3 = OH, R7 = CH2OMe, CH2O(CH2)2OMe, R8 = H, R14 = Me, X = CH2; R3 = OH, R7 = CH2OMe, R8 = R14 = H, X = CH2; R3 = OH, R7 = H, R8 = Me, R14 = Me, X = CH2; R3 = H, OMe, R7 = R8 = H, R14 = Me, X = (H)Me], were prepared for therapeutic use in the treatment of cancer. Discodermolide I (R3 = OH, R7 = R8 = H, R14 = Me, X = CH2) and its prepared analogs were assayed for inhibition of a number of cancer cell lines, such as MCF-7, A549 and SKOV-3.

REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

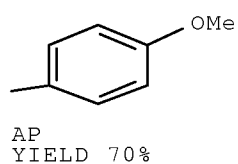
RX(12) OF 136 AN + AO ==> AP...



PAGE 1-A



PAGE 1-B



RX(12) RCT AN 870075-02-8

STAGE(1)

RGT AQ 109-72-8 BuLi, AR 7646-85-7 ZnCl2
SOL 60-29-7 Et2O, 109-66-0 Pentane
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) 5 minutes, -78 deg C
SUBSTAGE(3) -78 deg C -> room temperature
SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AO 212703-48-5
CAT 14221-01-3 Pd(PPh3)4
CON 15 hours, room temperature

STAGE(3)

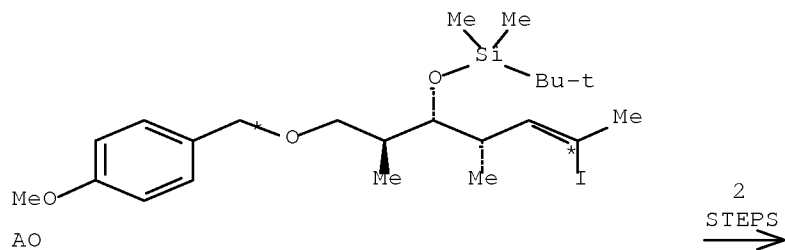
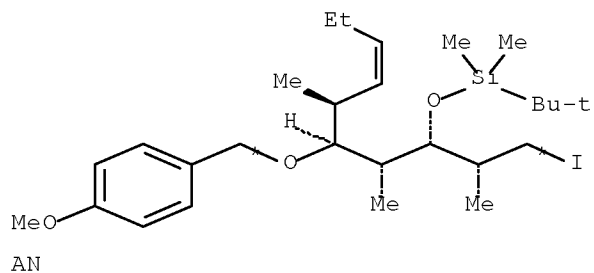
RGT P 7732-18-5 Water
CON room temperature

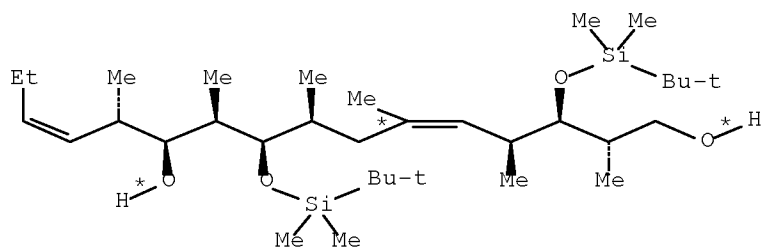
PRO AP 886845-60-9

NTE in the dark in stage 2

RX(42) OF 136 COMPOSED OF RX(12), RX(13)

RX(42) AN + AO ==> AU





AU
YIELD 63%

RX(12) RCT AN 870075-02-8

STAGE(1)

RGT AQ 109-72-8 BuLi, AR 7646-85-7 ZnCl₂
 SOL 60-29-7 Et₂O, 109-66-0 Pentane
 CON SUBSTAGE(1) room temperature -> -78 deg C
 SUBSTAGE(2) 5 minutes, -78 deg C
 SUBSTAGE(3) -78 deg C -> room temperature
 SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AO 212703-48-5
 CAT 14221-01-3 Pd(PPh₃)₄
 CON 15 hours, room temperature

STAGE(3)

RGT P 7732-18-5 Water
 CON room temperature

PRO AP 886845-60-9
 NTE in the dark in stage 2

RX(13) RCT AP 886845-60-9

STAGE(1)

RGT AV 84-58-2 DDQ
 SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
 CON 30 minutes, 0 deg C

STAGE(2)

RGT AW 16940-66-2 NaBH₄
 SOL 67-56-1 MeOH
 CON 10 minutes, room temperature

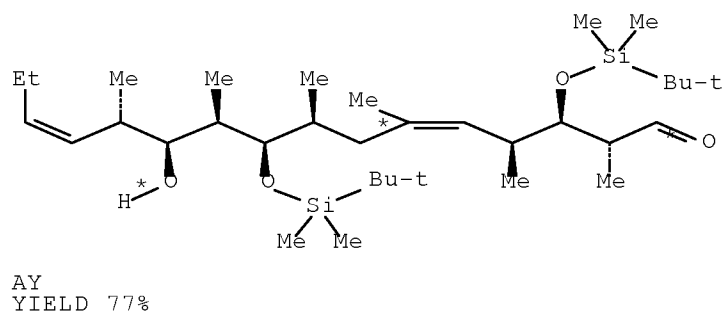
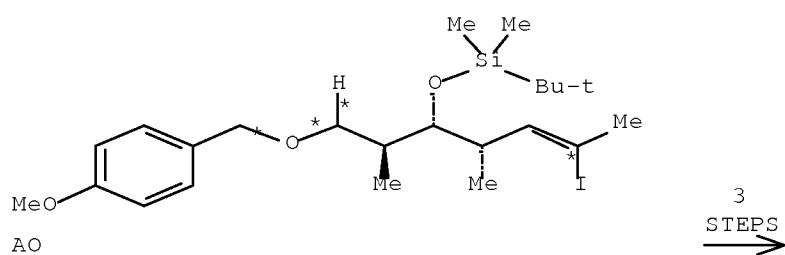
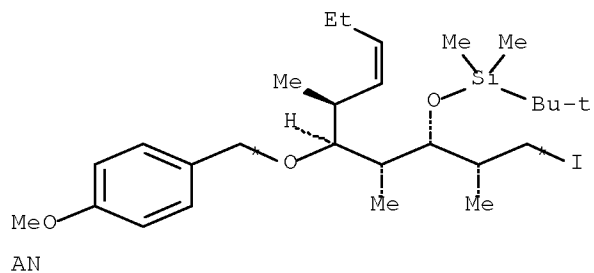
STAGE(3)

RGT AX 12125-02-9 NH₄Cl
 SOL 7732-18-5 Water
 CON room temperature

PRO AU 886845-61-0

RX(69) OF 136 COMPOSED OF RX(12), RX(13), RX(14)

RX(69) AN + AO ==> AY



RX(12) RCT AN 870075-02-8

STAGE(1)

RGT AQ 109-72-8 BuLi, AR 7646-85-7 ZnCl₂
 SOL 60-29-7 Et₂O, 109-66-0 Pentane
 CON SUBSTAGE(1) room temperature -> -78 deg C
 SUBSTAGE(2) 5 minutes, -78 deg C
 SUBSTAGE(3) -78 deg C -> room temperature
 SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AO 212703-48-5
 CAT 14221-01-3 Pd(PPh₃)₄

CON 15 hours, room temperature

STAGE(3)

RGT P 7732-18-5 Water

CON room temperature

PRO AP 886845-60-9

NTE in the dark in stage 2

RX(13) RCT AP 886845-60-9

STAGE(1)

RGT AV 84-58-2 DDQ

SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂

CON 30 minutes, 0 deg C

STAGE(2)

RGT AW 16940-66-2 NaBH₄

SOL 67-56-1 MeOH

CON 10 minutes, room temperature

STAGE(3)

RGT AX 12125-02-9 NH₄Cl

SOL 7732-18-5 Water

CON room temperature

PRO AU 886845-61-0

RX(14) RCT AU 886845-61-0

STAGE(1)

RGT AZ 2564-83-2 Me₄-piperidoxyl, BA 1321-07-9 Benzoic acid,
iodo-

SOL 75-09-2 CH₂Cl₂

CON 2.5 hours, room temperature

STAGE(2)

RGT AK 7772-98-7 Na₂S₂O₃

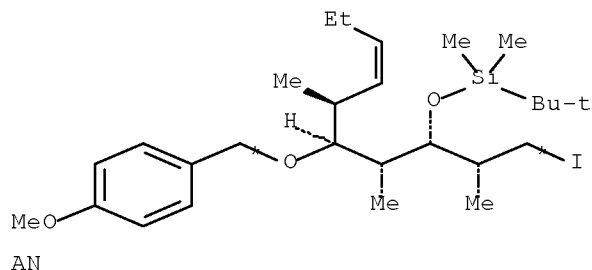
SOL 7732-18-5 Water

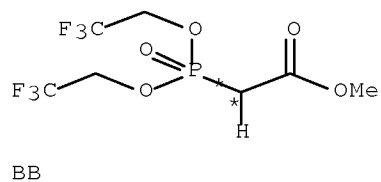
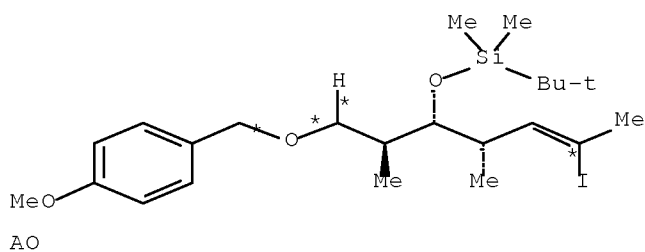
CON room temperature

PRO AY 886845-62-1

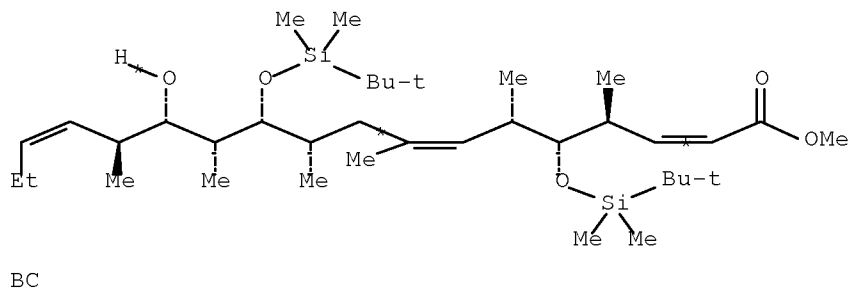
RX(71) OF 136 COMPOSED OF RX(12), RX(13), RX(14), RX(15)

RX(71) AN + AO + BB ==> BC





4
STEPS
→



RX(12) RCT AN 870075-02-8

STAGE(1)

RGT AQ 109-72-8 BuLi, AR 7646-85-7 ZnCl₂

SOL 60-29-7 Et₂O, 109-66-0 Pentane

CON SUBSTAGE(1) room temperature -> -78 deg C

SUBSTAGE(2) 5 minutes, -78 deg C

SUBSTAGE(3) -78 deg C -> room temperature

SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AO 212703-48-5

CAT 14221-01-3 Pd(PPh₃)₄

CON 15 hours, room temperature

STAGE(3)

RGT P 7732-18-5 Water

CON room temperature

PRO AP 886845-60-9
NTE in the dark in stage 2

RX(13) RCT AP 886845-60-9

STAGE(1)

RGT AV 84-58-2 DDQ
SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
CON 30 minutes, 0 deg C

STAGE(2)

RGT AW 16940-66-2 NaBH₄
SOL 67-56-1 MeOH
CON 10 minutes, room temperature

STAGE(3)

RGT AX 12125-02-9 NH₄Cl
SOL 7732-18-5 Water
CON room temperature

PRO AU 886845-61-0

RX(14) RCT AU 886845-61-0

STAGE(1)

RGT AZ 2564-83-2 Me₄-piperidoxyl, BA 1321-07-9 Benzoic acid,
iodo-
SOL 75-09-2 CH₂Cl₂
CON 2.5 hours, room temperature

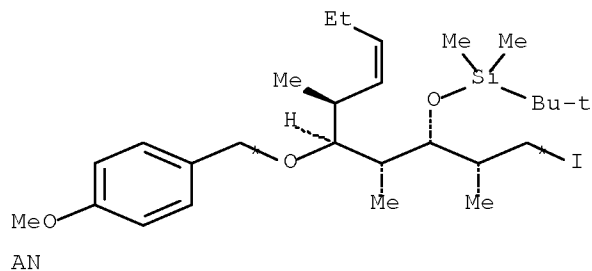
STAGE(2)

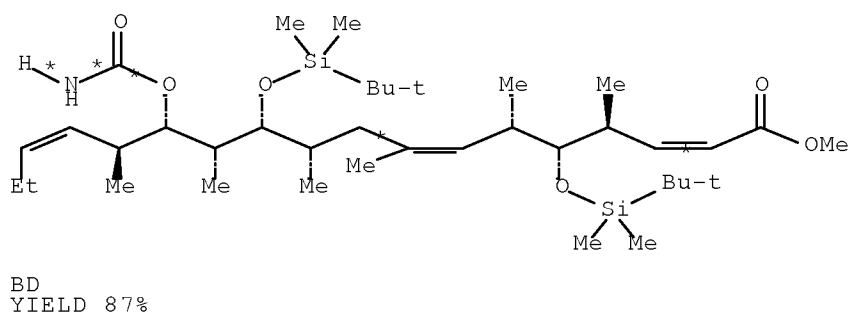
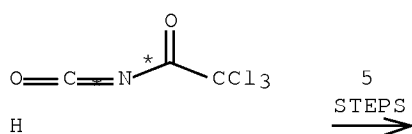
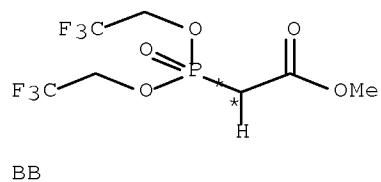
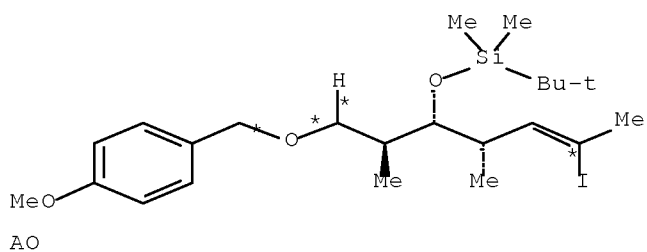
RGT AK 7772-98-7 Na₂S₂O₃
SOL 7732-18-5 Water
CON room temperature

PRO AY 886845-62-1

RX(15) RCT AY 886845-62-1, BB 88738-78-7
RGT J 584-08-7 K₂CO₃
PRO BC ~~886845-63-2~~
CAT 17455-13-9 18-Crown-6
SOL 108-88-3 PhMe

RX(98) OF 136 COMPOSED OF RX(12), RX(13), RX(14), RX(15), RX(16)
RX(98) AN + AO + BB + H ==> BD





RX(12) RCT AN 870075-02-8

STAGE(1)

RGT AQ 109-72-8 BuLi, AR 7646-85-7 ZnCl₂
 SOL 60-29-7 Et₂O, 109-66-0 Pentane
 CON SUBSTAGE(1) room temperature -> -78 deg C
 SUBSTAGE(2) 5 minutes, -78 deg C
 SUBSTAGE(3) -78 deg C -> room temperature
 SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AO 212703-48-5
 CAT 14221-01-3 Pd(PPh₃)₄
 CON 15 hours, room temperature

STAGE(3)
 RGT P 7732-18-5 Water
 CON room temperature

 PRO AP 886845-60-9
 NTE in the dark in stage 2

 RX(13) RCT AP 886845-60-9

 STAGE(1)
 RGT AV 84-58-2 DDQ
 SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
 CON 30 minutes, 0 deg C

 STAGE(2)
 RGT AW 16940-66-2 NaBH₄
 SOL 67-56-1 MeOH
 CON 10 minutes, room temperature

 STAGE(3)
 RGT AX 12125-02-9 NH₄Cl
 SOL 7732-18-5 Water
 CON room temperature

 PRO AU 886845-61-0

 RX(14) RCT AU 886845-61-0

 STAGE(1)
 RGT AZ 2564-83-2 Me₄-piperidoxyl, BA 1321-07-9 Benzoic acid,
 iodo-
 SOL 75-09-2 CH₂Cl₂
 CON 2.5 hours, room temperature

 STAGE(2)
 RGT AK 7772-98-7 Na₂S₂O₃
 SOL 7732-18-5 Water
 CON room temperature

 PRO AY 886845-62-1

 RX(15) RCT AY 886845-62-1, BB 88738-78-7
 RGT J 584-08-7 K₂CO₃
 PRO BC 886845-63-2
 CAT 17455-13-9 18-Crown-6
 SOL 108-88-3 PhMe

 RX(16) RCT BC 886845-63-2, H 3019-71-4

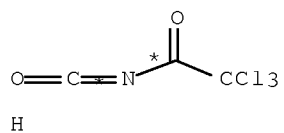
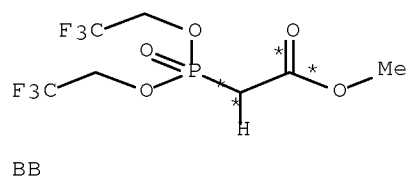
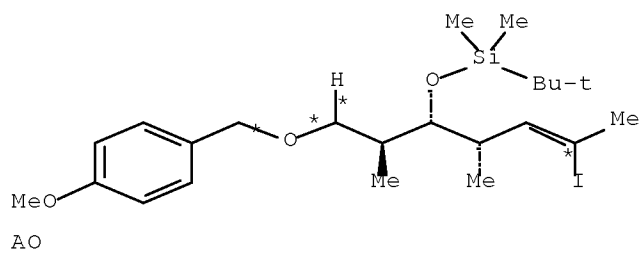
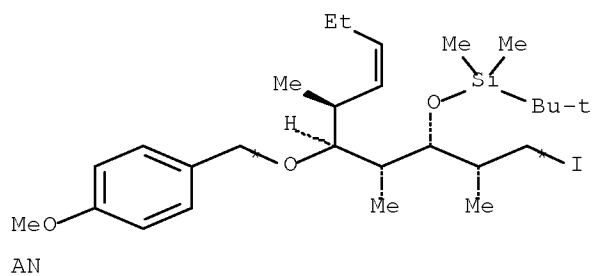
 STAGE(1)
 SOL 75-09-2 CH₂Cl₂
 CON 1 hour, room temperature

 STAGE(2)
 RGT J 584-08-7 K₂CO₃
 SOL 67-56-1 MeOH
 CON SUBSTAGE(1) room temperature -> 0 deg C
 SUBSTAGE(2) 1 hour, 0 deg C
 SUBSTAGE(3) 1.5 hours, room temperature

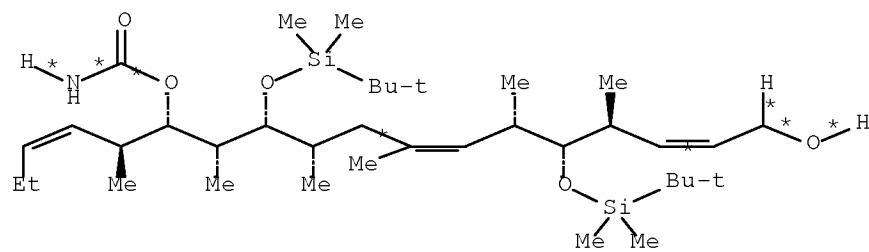
PRO BD 886845-64-3

RX(100) OF 136 COMPOSED OF RX(12), RX(13), RX(14), RX(15), RX(16), RX(17)

RX(100) AN + AO + BB + H ==> AI



6
STEPS
➔



YIELD 88%

RX(12) RCT AN 870075-02-8

STAGE(1)

RGT AQ 109-72-8 BuLi, AR 7646-85-7 ZnCl₂
SOL 60-29-7 Et₂O, 109-66-0 Pentane
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) 5 minutes, -78 deg C
SUBSTAGE(3) -78 deg C -> room temperature
SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AO 212703-48-5
CAT 14221-01-3 Pd(PPh₃)₄
CON 15 hours, room temperature

STAGE(3)

RGT P 7732-18-5 Water
CON room temperature

PRO AP 886845-60-9

NTE in the dark in stage 2

RX(13) RCT AP 886845-60-9

STAGE(1)

RGT AV 84-58-2 DDQ
SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
CON 30 minutes, 0 deg C

STAGE(2)

RGT AW 16940-66-2 NaBH₄
SOL 67-56-1 MeOH
CON 10 minutes, room temperature

STAGE(3)

RGT AX 12125-02-9 NH₄Cl
SOL 7732-18-5 Water
CON room temperature

PRO AU 886845-61-0

RX(14) RCT AU 886845-61-0

STAGE(1)

RGT AZ 2564-83-2 Me₄-piperidoxyl, BA 1321-07-9 Benzoic acid,
iodo-
SOL 75-09-2 CH₂Cl₂
CON 2.5 hours, room temperature

STAGE(2)

RGT AK 7772-98-7 Na₂S₂O₃
SOL 7732-18-5 Water
CON room temperature

PRO AY 886845-62-1

RX(15) RCT AY 886845-62-1, BB 88738-78-7

RX(16) RCT BC 886845-63-2, H 3019-71-4

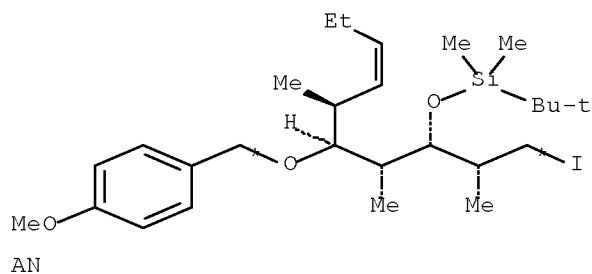
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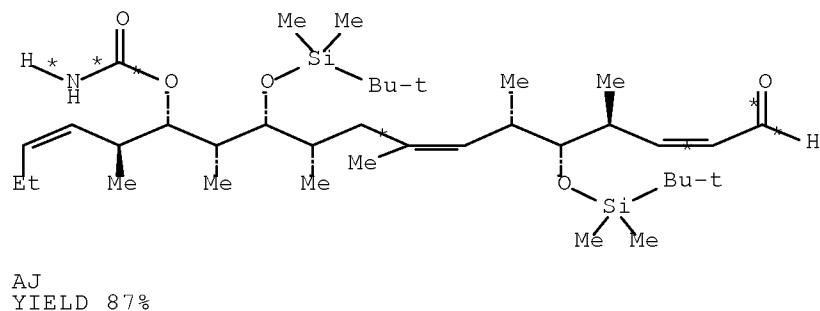
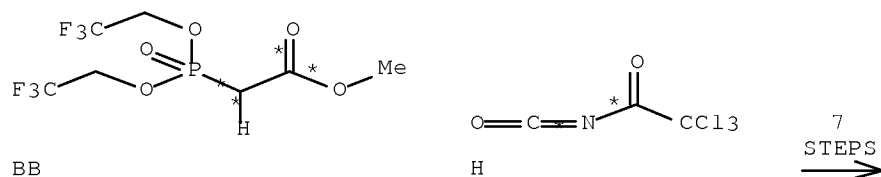
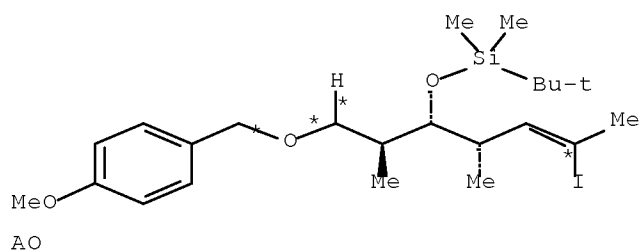
STAGE(2)
  RGT  J 584-08-7 K2CO3
  SOL  67-56-1 MeOH
  CON  SUBSTAGE(1) room temperature -> 0 deg C
        SUBSTAGE(2) 1 hour, 0 deg C
        SUBSTAGE(3) 1.5 hours, room temperature

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RX (17) RCT BD 886845-64-3

```
STAGE(2)
  RGT  O 304-59-6 Rochelle salt
  SOL  7732-18-5 Water
  CON  SUBSTAGE(1) 0 deg C
      SUBSTAGE(2) 1.5 deg C
```

$$\text{RX(103)} \quad \text{AN} + \text{AO} + \text{BB} + \text{H} \implies \text{AJ}$$




RX(12) RCT AN 870075-02-8

STAGE(1)

RGT AQ 109-72-8 BuLi, AR 7646-85-7 ZnCl₂
 SOL 60-29-7 Et₂O, 109-66-0 Pentane
 CON SUBSTAGE(1) room temperature -> -78 deg C
 SUBSTAGE(2) 5 minutes, -78 deg C
 SUBSTAGE(3) -78 deg C -> room temperature
 SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AO 212703-48-5
 CAT 14221-01-3 Pd(PPh₃)₄
 CON 15 hours, room temperature

STAGE(3)

RGT P 7732-18-5 Water

CON room temperature

PRO AP 886845-60-9
NTE in the dark in stage 2

RX(13) RCT AP 886845-60-9

STAGE(1)
RGT AV 84-58-2 DDQ
SOL 7732-18-5 Water, 75-09-2 CH2Cl2
CON 30 minutes, 0 deg C

STAGE(2)
RGT AW 16940-66-2 NaBH4
SOL 67-56-1 MeOH
CON 10 minutes, room temperature

STAGE(3)
RGT AX 12125-02-9 NH4Cl
SOL 7732-18-5 Water
CON room temperature

PRO AU 886845-61-0

RX(14) RCT AU 886845-61-0

STAGE(1)
RGT AZ 2564-83-2 Me4-piperidoxyl, BA 1321-07-9 Benzoic acid,
iodo-
SOL 75-09-2 CH2Cl2
CON 2.5 hours, room temperature

STAGE(2)
RGT AK 7772-98-7 Na2S2O3
SOL 7732-18-5 Water
CON room temperature

PRO AY 886845-62-1

RX(15) RCT AY 886845-62-1, BB 88738-78-7
RGT J 584-08-7 K2CO3
PRO BC 886845-63-2
CAT 17455-13-9 18-Crown-6
SOL 108-88-3 PhMe

RX(16) RCT BC 886845-63-2, H 3019-71-4

STAGE(1)
SOL 75-09-2 CH2Cl2
CON 1 hour, room temperature

STAGE(2)
RGT J 584-08-7 K2CO3
SOL 67-56-1 MeOH
CON SUBSTAGE(1) room temperature -> 0 deg C
SUBSTAGE(2) 1 hour, 0 deg C
SUBSTAGE(3) 1.5 hours, room temperature

PRO BD 886845-64-3

RX(17) RCT BD 886845-64-3

STAGE(1)

RGT N 1191-15-7 AlH(Bu-i)2
SOL 75-09-2 CH2Cl2, 110-54-3 Hexane
CON 25 minutes, -78 deg C

STAGE(2)

RGT O 304-59-6 Rochelle salt
SOL 7732-18-5 Water
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 1.5 deg C

PRO AI 886845-65-4

RX(9) RCT AI 886845-65-4

STAGE(1)

RGT S 144-55-8 NaHCO3, R 87413-09-0 Martin's reagent
SOL 75-09-2 CH2Cl2
CON 30 minutes, room temperature

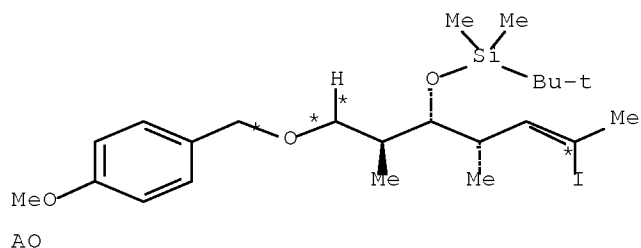
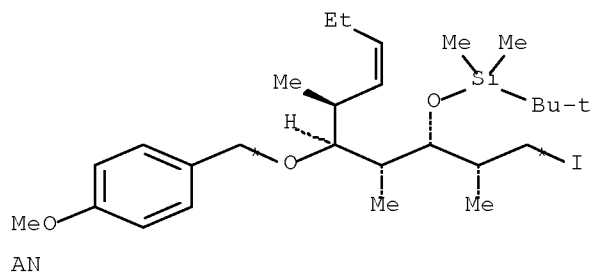
STAGE(2)

RGT AK 7772-98-7 Na2S2O3, S 144-55-8 NaHCO3
SOL 7732-18-5 Water
CON room temperature

PRO AJ 886845-57-4

RX(113) OF 136 COMPOSED OF RX(12), RX(13), RX(14), RX(15), RX(16), RX(17),
RX(9), RX(10)

RX(113) AN + AO + BB + H + AE ==> AL





8
STEPS
→

[illegible]CN(C)C

AL

RGT AQ 109-72-8 BuLi, AR 7646-85-7 ZnCl2
SOL 60-29-7 Et2O, 109-66-0 Pentane
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) 5 minutes, -78 deg C
SUBSTAGE(3) -78 deg C -> room temperature
SUBSTAGE(4) 1 hour, room temperature

STAGE(2)
RCT AO 212703-48-5
CAT 14221-01-3 Pd(PPh3)4
CON 15 hours, room temperature

STAGE(3)
RGT P 7732-18-5 Water
CON room temperature

PRO AP 886845-60-9
NTE in the dark in stage 2

RX(13) RCT AP 886845-60-9

STAGE(1)
RGT AV 84-58-2 DDQ
SOL 7732-18-5 Water, 75-09-2 CH2Cl2
CON 30 minutes, 0 deg C

STAGE(2)
RGT AW 16940-66-2 NaBH4
SOL 67-56-1 MeOH
CON 10 minutes, room temperature

STAGE(3)
RGT AX 12125-02-9 NH4Cl
SOL 7732-18-5 Water
CON room temperature

PRO AU 886845-61-0

RX(14) RCT AU 886845-61-0

STAGE(1)
RGT AZ 2564-83-2 Me4-piperidoxyl, BA 1321-07-9 Benzoic acid,
iodo-
SOL 75-09-2 CH2Cl2
CON 2.5 hours, room temperature

STAGE(2)
RGT AK 7772-98-7 Na2S2O3
SOL 7732-18-5 Water
CON room temperature

PRO AY 886845-62-1

RX(15) RCT AY 886845-62-1, BB 88738-78-7
RGT J 584-08-7 K2CO3
PRO BC 886845-63-2
CAT 17455-13-9 18-Crown-6
SOL 108-88-3 PhMe

RX(16) RCT BC 886845-63-2, H 3019-71-4

STAGE(1)
 SOL 75-09-2 CH2Cl2
 CON 1 hour, room temperature

STAGE(2)
 RGT J 584-08-7 K2CO3
 SOL 67-56-1 MeOH
 CON SUBSTAGE(1) room temperature -> 0 deg C
 SUBSTAGE(2) 1 hour, 0 deg C
 SUBSTAGE(3) 1.5 hours, room temperature

PRO BD 886845-64-3

RX(17) RCT BD 886845-64-3

STAGE(1)
 RGT N 1191-15-7 AlH(Bu-i)2
 SOL 75-09-2 CH2Cl2, 110-54-3 Hexane
 CON 25 minutes, -78 deg C

STAGE(2)
 RGT O 304-59-6 Rochelle salt
 SOL 7732-18-5 Water
 CON SUBSTAGE(1) 0 deg C
 SUBSTAGE(2) 1.5 deg C

PRO AI 886845-65-4

RX(9) RCT AI 886845-65-4

STAGE(1)
 RGT S 144-55-8 NaHCO3, R 87413-09-0 Martin's reagent
 SOL 75-09-2 CH2Cl2
 CON 30 minutes, room temperature

STAGE(2)
 RGT AK 7772-98-7 Na2S2O3, S 144-55-8 NaHCO3
 SOL 7732-18-5 Water
 CON room temperature

PRO AJ 886845-57-4

RX(10) RCT AE 193805-82-2

STAGE(1)
 RGT X 121-44-8 Et3N
 SOL 60-29-7 Et2O
 CON SUBSTAGE(1) 1 hour, 0 deg C
 SUBSTAGE(2) 0 deg C -> -78 deg C

STAGE(2)
 RCT AJ 886845-57-4
 SOL 60-29-7 Et2O
 CON SUBSTAGE(1) 3 hours, -78 deg C
 SUBSTAGE(2) 16 hours, -20 deg C
 SUBSTAGE(3) -20 deg C -> 0 deg C

STAGE(3)
 RGT L 67-56-1 MeOH

CON 0 deg C

STAGE(4)

RGT Y 7722-84-1 H2O2

SOL 7732-18-5 Water

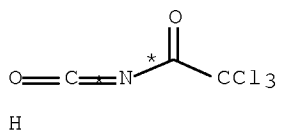
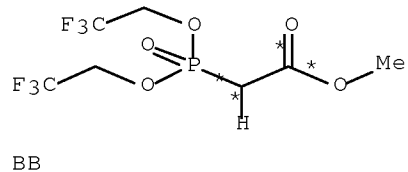
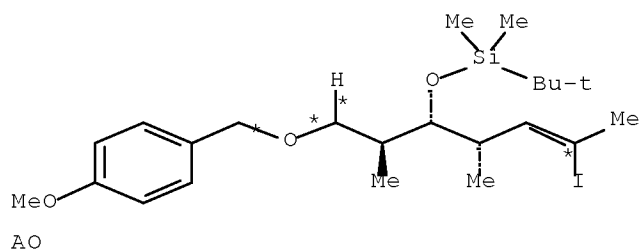
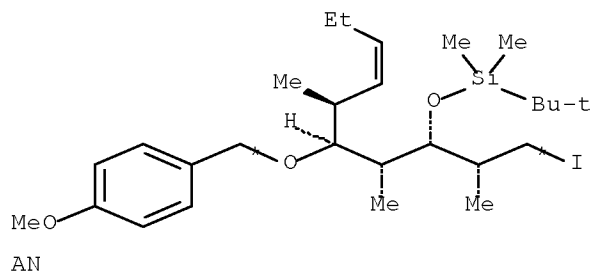
CON 1 hour, room temperature, pH 7

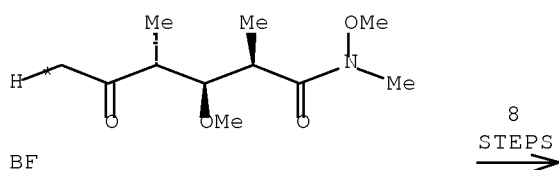
PRO AL 886845-58-5

NTE stereoselective, phosphate buffered used in stage 4, Aldol
reaction

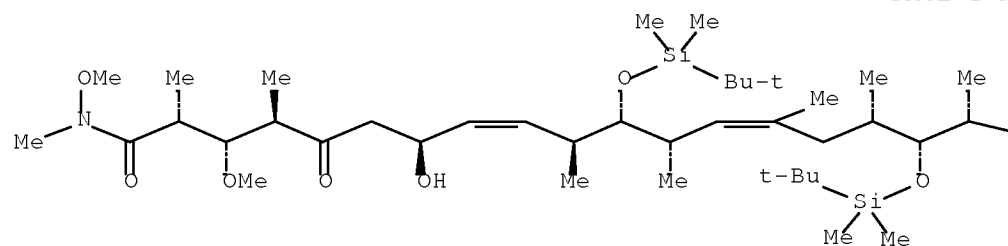
RX(114) OF 136 COMPOSED OF RX(12), RX(13), RX(14), RX(15), RX(16), RX(17),
RX(9), RX(18)

RX(114) AN + AO + BB + H + BF ==> BG

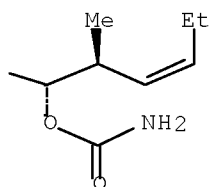




PAGE 1-A



PAGE 1-B



BG
 YIELD 87%

RX(12) RCT AN 870075-02-8

STAGE(1)

RGT AQ 109-72-8 BuLi, AR 7646-85-7 ZnCl2
 SOL 60-29-7 Et2O, 109-66-0 Pentane
 CON SUBSTAGE(1) room temperature -> -78 deg C
 SUBSTAGE(2) 5 minutes, -78 deg C
 SUBSTAGE(3) -78 deg C -> room temperature
 SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AO 212703-48-5
 CAT 14221-01-3 Pd(PPh3)4
 CON 15 hours, room temperature

STAGE(3)
 RGT P 7732-18-5 Water
 CON room temperature

 PRO AP 886845-60-9
 NTE in the dark in stage 2

 RX(13) RCT AP 886845-60-9

 STAGE(1)
 RGT AV 84-58-2 DDQ
 SOL 7732-18-5 Water, 75-09-2 CH2Cl2
 CON 30 minutes, 0 deg C

 STAGE(2)
 RGT AW 16940-66-2 NaBH4
 SOL 67-56-1 MeOH
 CON 10 minutes, room temperature

 STAGE(3)
 RGT AX 12125-02-9 NH4Cl
 SOL 7732-18-5 Water
 CON room temperature

 PRO AU 886845-61-0

 RX(14) RCT AU 886845-61-0

 STAGE(1)
 RGT AZ 2564-83-2 Me4-piperidoxyl, BA 1321-07-9 Benzoic acid,
 iodo-
 SOL 75-09-2 CH2Cl2
 CON 2.5 hours, room temperature

 STAGE(2)
 RGT AK 7772-98-7 Na2S2O3
 SOL 7732-18-5 Water
 CON room temperature

 PRO AY 886845-62-1

 RX(15) RCT AY 886845-62-1, BB 88738-78-7
 RGT J 584-08-7 K2CO3
 PRO BC 886845-63-2
 CAT 17455-13-9 18-Crown-6
 SOL 108-88-3 PhMe

 RX(16) RCT BC 886845-63-2, H 3019-71-4

 STAGE(1)
 SOL 75-09-2 CH2Cl2
 CON 1 hour, room temperature

 STAGE(2)
 RGT J 584-08-7 K2CO3
 SOL 67-56-1 MeOH
 CON SUBSTAGE(1) room temperature -> 0 deg C
 SUBSTAGE(2) 1 hour, 0 deg C
 SUBSTAGE(3) 1.5 hours, room temperature

PRO BD 886845-64-3

RX(17) RCT BD 886845-64-3

STAGE(1)

RGT N 1191-15-7 AlH(Bu-i)2
SOL 75-09-2 CH2Cl2, 110-54-3 Hexane
CON 25 minutes, -78 deg C

STAGE(2)

RGT O 304-59-6 Rochelle salt
SOL 7732-18-5 Water
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 1.5 deg C

PRO AI 886845-65-4

RX(9) RCT AI 886845-65-4

STAGE(1)

RGT S 144-55-8 NaHCO3, R 87413-09-0 Martin's reagent
SOL 75-09-2 CH2Cl2
CON 30 minutes, room temperature

STAGE(2)

RGT AK 7772-98-7 Na2S2O3, S 144-55-8 NaHCO3
SOL 7732-18-5 Water
CON room temperature

PRO AJ 886845-57-4

RX(18) RCT BF 884313-62-6

STAGE(1)

RGT W 112246-73-8 Bicycloheptylborane, X 121-44-8 Et3N
SOL 60-29-7 Et2O
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 0 deg C -> -78 deg C

STAGE(2)

RCT AJ 886845-57-4
SOL 60-29-7 Et2O
CON SUBSTAGE(1) 3 hours, -78 deg C
SUBSTAGE(2) 16 hours, -20 deg C
SUBSTAGE(3) -20 deg C -> 0 deg C

STAGE(3)

RGT L 67-56-1 MeOH
CON 0 deg C

STAGE(4)

RGT Y 7722-84-1 H2O2
SOL 7732-18-5 Water
CON 1 hour, room temperature, pH 7

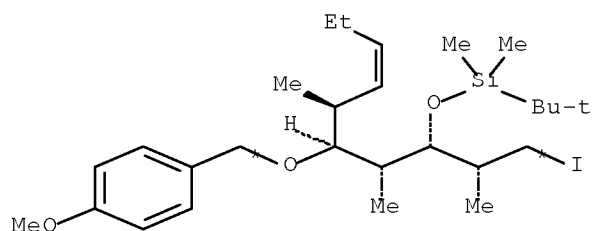
PRO BG 886845-66-5

NTE stereoselective, phosphate buffered solution used in stage 4

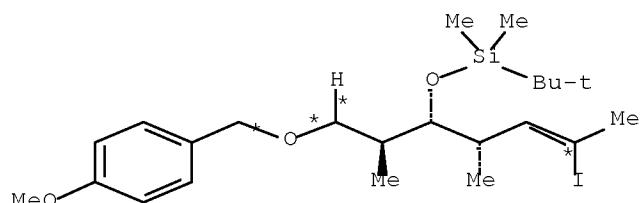
RX(115) OF 136 COMPOSED OF RX(12), RX(13), RX(14), RX(15), RX(16), RX(17),

RX(9), RX(28)

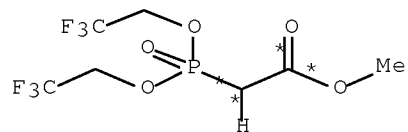
RX(115) AN + AO + BB + H + BZ ==> BX



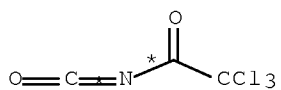
AN



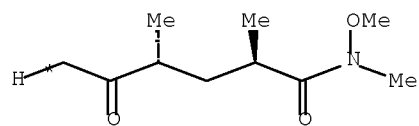
AO



BB

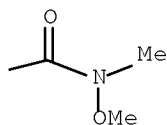
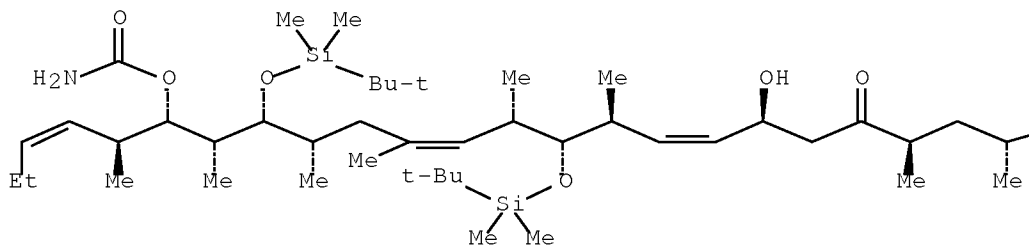


H



BZ

8
STEPS
➔



BX
YIELD 83%

RX(12) RCT AN 870075-02-8

STAGE(1)

RGT AQ 109-72-8 BuLi, AR 7646-85-7 ZnCl2
 SOL 60-29-7 Et2O, 109-66-0 Pentane
 CON SUBSTAGE(1) room temperature -> -78 deg C
 SUBSTAGE(2) 5 minutes, -78 deg C
 SUBSTAGE(3) -78 deg C -> room temperature
 SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AO 212703-48-5
 CAT 14221-01-3 Pd(PPh3)4
 CON 15 hours, room temperature

STAGE(3)

RGT P 7732-18-5 Water
 CON room temperature

PRO AP 886845-60-9
 NTE in the dark in stage 2

RX(13) RCT AP 886845-60-9

STAGE(1)

RGT AV 84-58-2 DDQ
 SOL 7732-18-5 Water, 75-09-2 CH2Cl2
 CON 30 minutes, 0 deg C

STAGE(2)

RGT AW 16940-66-2 NaBH4
SOL 67-56-1 MeOH
CON 10 minutes, room temperature

STAGE(3)

RGT AX 12125-02-9 NH4Cl
SOL 7732-18-5 Water
CON room temperature

PRO AU 886845-61-0

RX(14) RCT AU 886845-61-0

STAGE(1)

RGT AZ 2564-83-2 Me4-piperidoxyl, BA 1321-07-9 Benzoic acid,
iodo-
SOL 75-09-2 CH2Cl2
CON 2.5 hours, room temperature

STAGE(2)

RGT AK 7772-98-7 Na2S2O3
SOL 7732-18-5 Water
CON room temperature

PRO AY 886845-62-1

RX(15) RCT AY 886845-62-1, BB 88738-78-7
RGT J 584-08-7 K2CO3
PRO BC 886845-63-2
CAT 17455-13-9 18-Crown-6
SOL 108-88-3 PhMe

RX(16) RCT BC 886845-63-2, H 3019-71-4

STAGE(1)

SOL 75-09-2 CH2Cl2
CON 1 hour, room temperature

STAGE(2)

RGT J 584-08-7 K2CO3
SOL 67-56-1 MeOH
CON SUBSTAGE(1) room temperature -> 0 deg C
SUBSTAGE(2) 1 hour, 0 deg C
SUBSTAGE(3) 1.5 hours, room temperature

PRO BD 886845-64-3

RX(17) RCT BD 886845-64-3

STAGE(1)

RGT N 1191-15-7 AlH(Bu-i)2
SOL 75-09-2 CH2Cl2, 110-54-3 Hexane
CON 25 minutes, -78 deg C

STAGE(2)

RGT O 304-59-6 Rochelle salt
SOL 7732-18-5 Water
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 1.5 deg C

PRO AI 886845-65-4

RX(9) RCT AI 886845-65-4

STAGE(1)

RGT S 144-55-8 NaHCO₃, R 87413-09-0 Martin's reagent
SOL 75-09-2 CH₂Cl₂
CON 30 minutes, room temperature

STAGE(2)

RGT AK 7772-98-7 Na₂S₂O₃, S 144-55-8 NaHCO₃
SOL 7732-18-5 Water
CON room temperature

PRO AJ 886845-57-4

RX(28) RCT BZ 884313-63-7

STAGE(1)

RGT W 112246-73-8 Bicycloheptylborane, X 121-44-8 Et₃N
SOL 60-29-7 Et₂O
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 0 deg C -> -78 deg C

STAGE(2)

RCT AJ 886845-57-4
SOL 60-29-7 Et₂O
CON SUBSTAGE(1) 3 hours, -78 deg C
SUBSTAGE(2) 16 hours, -20 deg C
SUBSTAGE(3) -20 deg C -> 0 deg C

STAGE(3)

RGT L 67-56-1 MeOH
CON 0 deg C

STAGE(4)

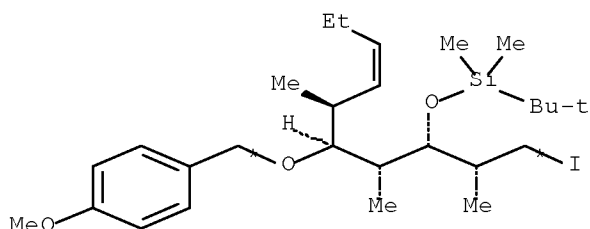
RGT Y 7722-84-1 H₂O₂
SOL 7732-18-5 Water
CON 1 hour, room temperature, pH 7

PRO BX 886845-76-7

NTE stereoselective, phosphate buffered solution used in stage 4

RX(130) OF 136 COMPOSED OF RX(12), RX(13), RX(14), RX(15), RX(16), RX(17),
RX(9), RX(10), RX(11)

RX(130) AN + AO + BB + H + AE ==> AM



AN



RX(12) RCT AN 870075--02--8

STAGE(1)
 RGT AQ 109-72-8 BuLi, AR 7646-85-7 ZnCl2
 SOL 60-29-7 Et2O, 109-66-0 Pentane
 CON SUBSTAGE(1) room temperature -> -78 deg C
 SUBSTAGE(2) 5 minutes, -78 deg C
 SUBSTAGE(3) -78 deg C -> room temperature
 SUBSTAGE(4) 1 hour, room temperature

STAGE(2)
 RCT AO 212703-48-5
 CAT 14221-01-3 Pd(PPh3)4
 CON 15 hours, room temperature

STAGE(3)
 RGT P 7732-18-5 Water
 CON room temperature

PRO AP 886845-60-9
 NTE in the dark in stage 2

RX(13) RCT AP 886845-60-9

 STAGE(1)
 RGT AV 84-58-2 DDQ
 SOL 7732-18-5 Water, 75-09-2 CH2Cl2
 CON 30 minutes, 0 deg C

 STAGE(2)
 RGT AW 16940-66-2 NaBH4
 SOL 67-56-1 MeOH
 CON 10 minutes, room temperature

 STAGE(3)
 RGT AX 12125-02-9 NH4Cl
 SOL 7732-18-5 Water
 CON room temperature

PRO AU 886845-61-0

RX(14) RCT AU 886845-61-0

 STAGE(1)
 RGT AZ 2564-83-2 Me4-piperidoxyl, BA 1321-07-9 Benzoic acid,
 iodo-
 SOL 75-09-2 CH2Cl2
 CON 2.5 hours, room temperature

 STAGE(2)
 RGT AK 7772-98-7 Na2S2O3
 SOL 7732-18-5 Water
 CON room temperature

PRO AY 886845-62-1

RX(15) RCT AY 886845-62-1, BB 88738-78-7
 RGT J 584-08-7 K2CO3
 PRO BC 886845-63-2
 CAT 17455-13-9 18-Crown-6
 SOL 108-88-3 PhMe

RX(16) RCT BC 886845-63-2, H 3019-71-4

STAGE(1)
SOL 75-09-2 CH₂Cl₂
CON 1 hour, room temperature

STAGE(2)
RGT J 584-08-7 K₂CO₃
SOL 67-56-1 MeOH
CON SUBSTAGE(1) room temperature -> 0 deg C
SUBSTAGE(2) 1 hour, 0 deg C
SUBSTAGE(3) 1.5 hours, room temperature

PRO BD 886845-64-3

RX(17) RCT BD 886845-64-3

STAGE(1)
RGT N 1191-15-7 AlH(Bu-i)₂
SOL 75-09-2 CH₂Cl₂, 110-54-3 Hexane
CON 25 minutes, -78 deg C

STAGE(2)
RGT O 304-59-6 Rochelle salt
SOL 7732-18-5 Water
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 1.5 deg C

PRO AI 886845-65-4

RX(9) RCT AI 886845-65-4

STAGE(1)
RGT S 144-55-8 NaHCO₃, R 87413-09-0 Martin's reagent
SOL 75-09-2 CH₂Cl₂
CON 30 minutes, room temperature

STAGE(2)
RGT AK 7772-98-7 Na₂S₂O₃, S 144-55-8 NaHCO₃
SOL 7732-18-5 Water
CON room temperature

PRO AJ 886845-57-4

RX(10) RCT AE 193805-82-2

STAGE(1)
RGT X 121-44-8 Et₃N
SOL 60-29-7 Et₂O
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 0 deg C -> -78 deg C

STAGE(2)
RCT AJ 886845-57-4
SOL 60-29-7 Et₂O
CON SUBSTAGE(1) 3 hours, -78 deg C
SUBSTAGE(2) 16 hours, -20 deg C
SUBSTAGE(3) -20 deg C -> 0 deg C

STAGE(3)

RGT L 67-56-1 MeOH
CON 0 deg C

STAGE(4)

RGT Y 7722-84-1 H2O2
SOL 7732-18-5 Water
CON 1 hour, room temperature, pH 7

PRO AL 886845-58-5

NTE stereoselective, phosphate buffered used in stage 4, Aldol
reaction

RX(11)

STAGE(1)

RGT AB 109704-53-2 Me4N.(AcO)3BH, AC 64-19-7 AcOH
SOL 75-05-8 MeCN
CON SUBSTAGE(1) 30 minutes, room temperature
SUBSTAGE(2) room temperature -> -30 deg C

STAGE(2)

RGT AL 886845-58-5
RGT AC 64-19-7 AcOH
SOL 75-05-8 MeCN
CON SUBSTAGE(1) 30 minutes, -30 deg C
SUBSTAGE(2) 1 hour, 0 deg C

STAGE(3)

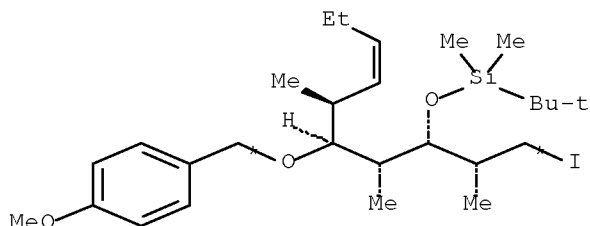
RGT O 304-59-6 Rochelle salt
SOL 7732-18-5 Water
CON 5 minutes

PRO AM 886845-59-6

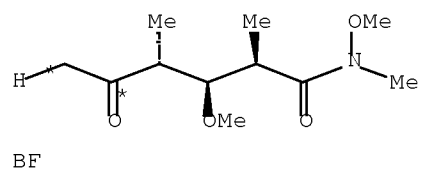
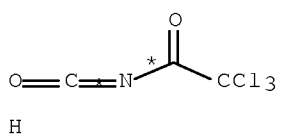
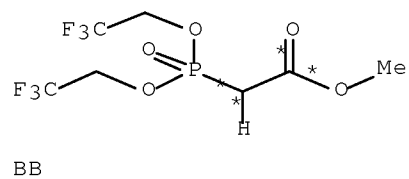
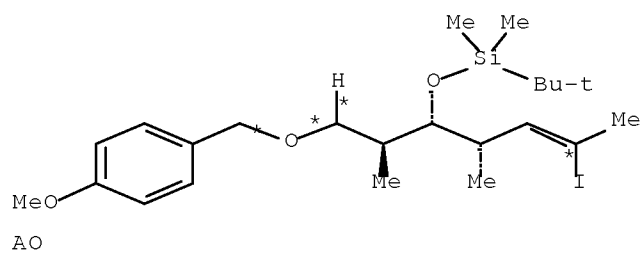
NTE stereoselective

RX(131) OF 136 COMPOSED OF RX(12), RX(13), RX(14), RX(15), RX(16), RX(17),
RX(9), RX(18), RX(19)

RX(131) AN + AO + BB + H + BF ==> BH

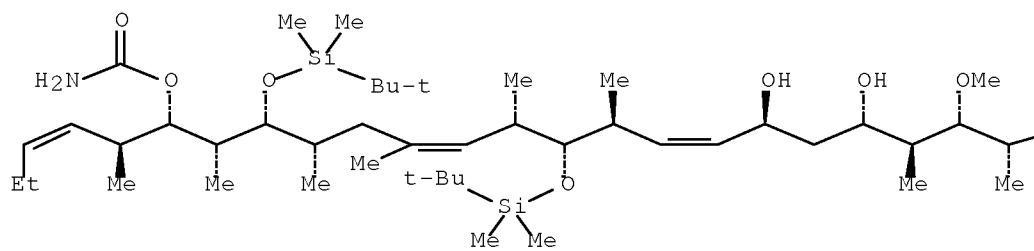


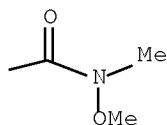
AN



9
 STEPS

PAGE 1-A





BH
YIELD 81%

RX(12) RCT AN 870075-02-8

STAGE(1)

RGT AQ 109-72-8 BuLi, AR 7646-85-7 ZnCl₂
SOL 60-29-7 Et₂O, 109-66-0 Pentane
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) 5 minutes, -78 deg C
SUBSTAGE(3) -78 deg C -> room temperature
SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AO 212703-48-5
CAT 14221-01-3 Pd(PPh₃)₄
CON 15 hours, room temperature

STAGE(3)

RGT P 7732-18-5 Water
CON room temperature

PRO AP 886845-60-9
NTE in the dark in stage 2

RX(13) RCT AP 886845-60-9

STAGE(1)

RGT AV 84-58-2 DDQ
SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
CON 30 minutes, 0 deg C

STAGE(2)

RGT AW 16940-66-2 NaBH₄
SOL 67-56-1 MeOH
CON 10 minutes, room temperature

STAGE(3)

RGT AX 12125-02-9 NH₄Cl
SOL 7732-18-5 Water
CON room temperature

PRO AU 886845-61-0

RX(14) RCT AU 886845-61-0

STAGE(1)

RGT AZ 2564-83-2 Me₄-piperidoxyl, BA 1321-07-9 Benzoic acid,

iodo-
SOL 75-09-2 CH₂Cl₂
CON 2.5 hours, room temperature

STAGE(2)
RGT AK 7772-98-7 Na₂S₂O₃
SOL 7732-18-5 Water
CON room temperature

PRO AY 886845-62-1

RX(15) RCT AY 886845-62-1, BB 88738-78-7
RGT J 584-08-7 K₂CO₃
PRO BC 886845-63-2
CAT 17455-13-9 18-Crown-6
SOL 108-88-3 PhMe

RX(16) RCT BC 886845-63-2, H 3019-71-4

STAGE(1)
SOL 75-09-2 CH₂Cl₂
CON 1 hour, room temperature

STAGE(2)
RGT J 584-08-7 K₂CO₃
SOL 67-56-1 MeOH
CON SUBSTAGE(1) room temperature -> 0 deg C
SUBSTAGE(2) 1 hour, 0 deg C
SUBSTAGE(3) 1.5 hours, room temperature

PRO BD 886845-64-3

RX(17) RCT BD 886845-64-3

STAGE(1)
RGT N 1191-15-7 AlH(Bu-i)₂
SOL 75-09-2 CH₂Cl₂, 110-54-3 Hexane
CON 25 minutes, -78 deg C

STAGE(2)
RGT O 304-59-6 Rochelle salt
SOL 7732-18-5 Water
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 1.5 deg C

PRO AI 886845-65-4

RX(9) RCT AI 886845-65-4

STAGE(1)
RGT S 144-55-8 NaHCO₃, R 87413-09-0 Martin's reagent
SOL 75-09-2 CH₂Cl₂
CON 30 minutes, room temperature

STAGE(2)
RGT AK 7772-98-7 Na₂S₂O₃, S 144-55-8 NaHCO₃
SOL 7732-18-5 Water
CON room temperature

PRO AJ 886845-57-4

RX(18) RCT BF 884313-62-6

STAGE(1)

RGT W 112246-73-8 Bicycloheptylborane, X 121-44-8 Et3N
SOL 60-29-7 Et2O
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 0 deg C -> -78 deg C

STAGE(2)

RCT AJ 886845-57-4
SOL 60-29-7 Et2O
CON SUBSTAGE(1) 3 hours, -78 deg C
SUBSTAGE(2) 16 hours, -20 deg C
SUBSTAGE(3) -20 deg C -> 0 deg C

STAGE(3)

RGT L 67-56-1 MeOH
CON 0 deg C

STAGE(4)

RGT Y 7722-84-1 H2O2
SOL 7732-18-5 Water
CON 1 hour, room temperature, pH 7

PRO BG 886845-66-5

NTE stereoselective, phosphate buffered solution used in stage 4

RX(19)

STAGE(1)

RGT AB 109704-53-2 Me4N.(AcO)3BH, AC 64-19-7 AcOH
SOL 75-05-8 MeCN
CON SUBSTAGE(1) 30 minutes, room temperature
SUBSTAGE(2) room temperature -> -30 deg C

STAGE(2)

RCT BG 886845-66-5
RGT AC 64-19-7 AcOH
SOL 75-05-8 MeCN
CON SUBSTAGE(1) 30 minutes, -30 deg C
SUBSTAGE(2) 1 hour, 0 deg C

STAGE(3)

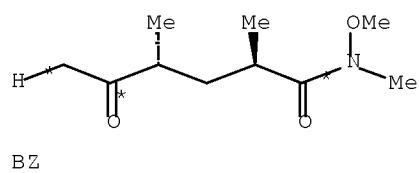
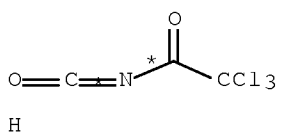
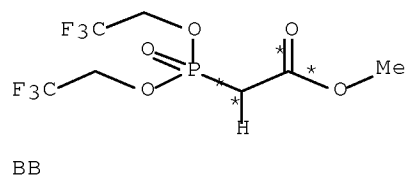
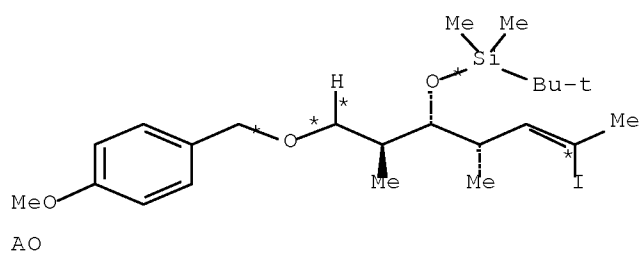
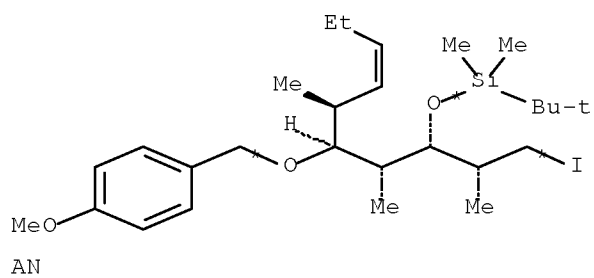
RGT O 304-59-6 Rochelle salt
SOL 7732-18-5 Water
CON 5 minutes

PRO BH 886845-67-6

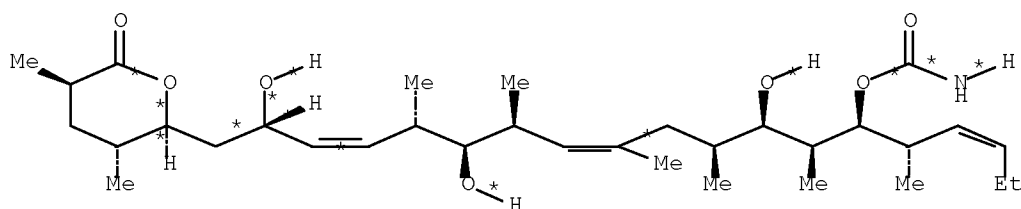
NTE stereoselective

RX(132) OF 136 COMPOSED OF RX(12), RX(13), RX(14), RX(15), RX(16), RX(17),
RX(9), RX(28), RX(27)

RX(132) AN + AO + BB + H + BZ ==> BY



9
 STEPS
 →



BY
YIELD 6%

RX(12) RCT AN 870075-02-8

STAGE(1)

RGT AQ 109-72-8 BuLi, AR 7646-85-7 ZnCl₂
SOL 60-29-7 Et₂O, 109-66-0 Pentane
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) 5 minutes, -78 deg C
SUBSTAGE(3) -78 deg C -> room temperature
SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AO 212703-48-5
CAT 14221-01-3 Pd(PPh₃)₄
CON 15 hours, room temperature

STAGE(3)

RGT P 7732-18-5 Water
CON room temperature

PRO AP 886845-60-9
NTE in the dark in stage 2

RX(13) RCT AP 886845-60-9

STAGE(1)

RGT AV 84-58-2 DDQ
SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
CON 30 minutes, 0 deg C

STAGE(2)

RGT AW 16940-66-2 NaBH₄
SOL 67-56-1 MeOH
CON 10 minutes, room temperature

STAGE(3)

RGT AX 12125-02-9 NH₄Cl
SOL 7732-18-5 Water
CON room temperature

PRO AU 886845-61-0

RX(14) RCT AU 886845-61-0

STAGE(1)

RGT AZ 2564-83-2 Me₄-piperidoxyl, BA 1321-07-9 Benzoic acid,

iodo-
SOL 75-09-2 CH₂Cl₂
CON 2.5 hours, room temperature

STAGE(2)
RGT AK 7772-98-7 Na₂S₂O₃
SOL 7732-18-5 Water
CON room temperature

PRO AY 886845-62-1

RX(15) RCT AY 886845-62-1, BB 88738-78-7
RGT J 584-08-7 K₂CO₃
PRO BC 886845-63-2
CAT 17455-13-9 18-Crown-6
SOL 108-88-3 PhMe

RX(16) RCT BC 886845-63-2, H 3019-71-4

STAGE(1)
SOL 75-09-2 CH₂Cl₂
CON 1 hour, room temperature

STAGE(2)
RGT J 584-08-7 K₂CO₃
SOL 67-56-1 MeOH
CON SUBSTAGE(1) room temperature -> 0 deg C
SUBSTAGE(2) 1 hour, 0 deg C
SUBSTAGE(3) 1.5 hours, room temperature

PRO BD 886845-64-3

RX(17) RCT BD 886845-64-3

STAGE(1)
RGT N 1191-15-7 AlH(Bu-i)₂
SOL 75-09-2 CH₂Cl₂, 110-54-3 Hexane
CON 25 minutes, -78 deg C

STAGE(2)
RGT O 304-59-6 Rochelle salt
SOL 7732-18-5 Water
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 1.5 deg C

PRO AI 886845-65-4

RX(9) RCT AI 886845-65-4

STAGE(1)
RGT S 144-55-8 NaHCO₃, R 87413-09-0 Martin's reagent
SOL 75-09-2 CH₂Cl₂
CON 30 minutes, room temperature

STAGE(2)
RGT AK 7772-98-7 Na₂S₂O₃, S 144-55-8 NaHCO₃
SOL 7732-18-5 Water
CON room temperature

PRO AJ 886845-57-4

RX(28) RCT BZ 884313-63-7

STAGE(1)

RGT W 112246-73-8 Bicycloheptylborane, X 121-44-8 Et3N
SOL 60-29-7 Et2O
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 0 deg C -> -78 deg C

STAGE(2)

RCT AJ 886845-57-4
SOL 60-29-7 Et2O
CON SUBSTAGE(1) 3 hours, -78 deg C
SUBSTAGE(2) 16 hours, -20 deg C
SUBSTAGE(3) -20 deg C -> 0 deg C

STAGE(3)

RGT L 67-56-1 MeOH
CON 0 deg C

STAGE(4)

RGT Y 7722-84-1 H2O2
SOL 7732-18-5 Water
CON 1 hour, room temperature, pH 7

PRO BX 886845-76-7

NTE stereoselective, phosphate buffered solution used in stage 4

RX(27)

STAGE(1)

RGT AB 109704-53-2 Me4N.(AcO)3BH, AC 64-19-7 AcOH
SOL 75-05-8 MeCN
CON SUBSTAGE(1) 30 minutes, room temperature
SUBSTAGE(2) room temperature -> -30 deg C

STAGE(2)

RCT BX 886845-76-7
RGT AC 64-19-7 AcOH
SOL 75-05-8 MeCN
CON SUBSTAGE(1) 30 minutes, -30 deg C
SUBSTAGE(2) 1 hour, 0 deg C

STAGE(3)

RGT O 304-59-6 Rochelle salt
SOL 7732-18-5 Water
CON 5 minutes

STAGE(4)

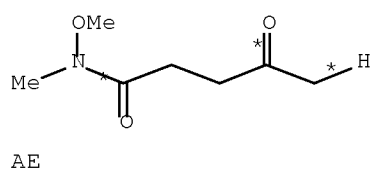
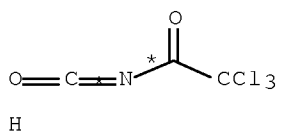
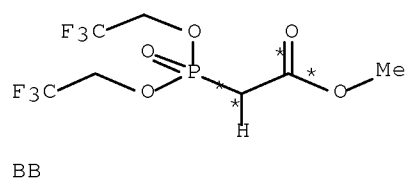
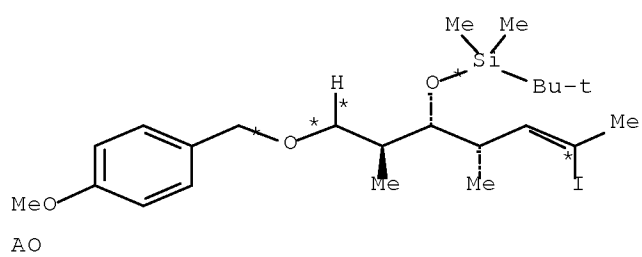
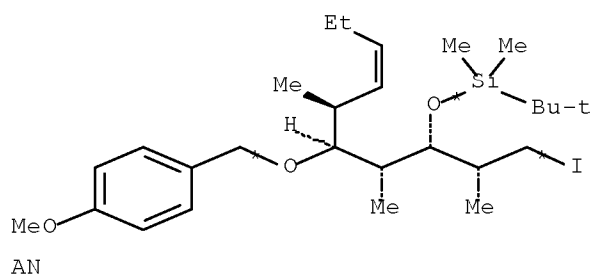
RGT BT 7647-01-0 HCl
SOL 7732-18-5 Water, 67-56-1 MeOH
CON 3 hours, room temperature

PRO BY 886845-75-6

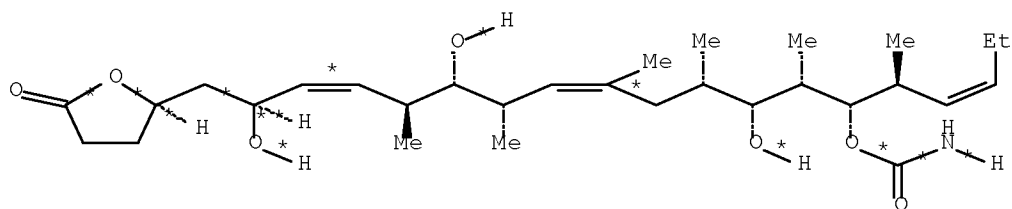
NTE stereoselective, incremental addition of the reagent in stage 4

RX(135) OF 136 COMPOSED OF RX(12), RX(13), RX(14), RX(15), RX(16), RX(17),
RX(9), RX(10), RX(11), RX(25)

RX(135) AN + AO + BB + H + AE ==> EV



10
 STEPS



BV
YIELD 57%

RX(12) RCT AN 870075-02-8

STAGE(1)

RGT AQ 109-72-8 BuLi, AR 7646-85-7 ZnCl₂
SOL 60-29-7 Et₂O, 109-66-0 Pentane
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) 5 minutes, -78 deg C
SUBSTAGE(3) -78 deg C -> room temperature
SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AO 212703-48-5
CAT 14221-01-3 Pd(PPh₃)₄
CON 15 hours, room temperature

STAGE(3)

RGT P 7732-18-5 Water
CON room temperature

PRO AP 886845-60-9
NTE in the dark in stage 2

RX(13) RCT AP 886845-60-9

STAGE(1)

RGT AV 84-58-2 DDQ
SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
CON 30 minutes, 0 deg C

STAGE(2)

RGT AW 16940-66-2 NaBH₄
SOL 67-56-1 MeOH
CON 10 minutes, room temperature

STAGE(3)

RGT AX 12125-02-9 NH₄Cl
SOL 7732-18-5 Water
CON room temperature

PRO AU 886845-61-0

RX(14) RCT AU 886845-61-0

STAGE(1)

RGT AZ 2564-83-2 Me₄-piperidoxyl, BA 1321-07-9 Benzoic acid,

iodo-
SOL 75-09-2 CH₂Cl₂
CON 2.5 hours, room temperature

STAGE(2)
RGT AK 7772-98-7 Na₂S₂O₃
SOL 7732-18-5 Water
CON room temperature

PRO AY 886845-62-1

RX(15) RCT AY 886845-62-1, BB 88738-78-7
RGT J 584-08-7 K₂CO₃
PRO BC 886845-63-2
CAT 17455-13-9 18-Crown-6
SOL 108-88-3 PhMe

RX(16) RCT BC 886845-63-2, H 3019-71-4

STAGE(1)
SOL 75-09-2 CH₂Cl₂
CON 1 hour, room temperature

STAGE(2)
RGT J 584-08-7 K₂CO₃
SOL 67-56-1 MeOH
CON SUBSTAGE(1) room temperature -> 0 deg C
SUBSTAGE(2) 1 hour, 0 deg C
SUBSTAGE(3) 1.5 hours, room temperature

PRO BD 886845-64-3

RX(17) RCT BD 886845-64-3

STAGE(1)
RGT N 1191-15-7 AlH(Bu-i)₂
SOL 75-09-2 CH₂Cl₂, 110-54-3 Hexane
CON 25 minutes, -78 deg C

STAGE(2)
RGT O 304-59-6 Rochelle salt
SOL 7732-18-5 Water
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 1.5 deg C

PRO AI 886845-65-4

RX(9) RCT AI 886845-65-4

STAGE(1)
RGT S 144-55-8 NaHCO₃, R 87413-09-0 Martin's reagent
SOL 75-09-2 CH₂Cl₂
CON 30 minutes, room temperature

STAGE(2)
RGT AK 7772-98-7 Na₂S₂O₃, S 144-55-8 NaHCO₃
SOL 7732-18-5 Water
CON room temperature

PRO AJ 886845-57-4

RX(10) RCT AE 193805-82-2

STAGE(1)

RGT X 121-44-8 Et3N

SOL 60-29-7 Et2O

CON SUBSTAGE(1) 1 hour, 0 deg C

SUBSTAGE(2) 0 deg C -> -78 deg C

STAGE(2)

RCT AJ 886845-57-4

SOL 60-29-7 Et2O

CON SUBSTAGE(1) 3 hours, -78 deg C

SUBSTAGE(2) 16 hours, -20 deg C

SUBSTAGE(3) -20 deg C -> 0 deg C

STAGE(3)

RGT L 67-56-1 MeOH

CON 0 deg C

STAGE(4)

RGT Y 7722-84-1 H2O2

SOL 7732-18-5 Water

CON 1 hour, room temperature, pH 7

PRO AL 886845-58-5

NTE stereoselective, phosphate buffered used in stage 4, Aldol reaction

RX(11)

STAGE(1)

RGT AB 109704-53-2 Me4N.(AcO)3BH, AC 64-19-7 AcOH

SOL 75-05-8 MeCN

CON SUBSTAGE(1) 30 minutes, room temperature

SUBSTAGE(2) room temperature -> -30 deg C

STAGE(2)

RCT AL 886845-58-5

RGT AC 64-19-7 AcOH

SOL 75-05-8 MeCN

CON SUBSTAGE(1) 30 minutes, -30 deg C

SUBSTAGE(2) 1 hour, 0 deg C

STAGE(3)

RGT O 304-59-6 Rochelle salt

SOL 7732-18-5 Water

CON 5 minutes

PRO AM 886845-59-6

NTE stereoselective

RX(25)

RCT AM 886845-59-6

RGT BT 7647-01-0 HCl

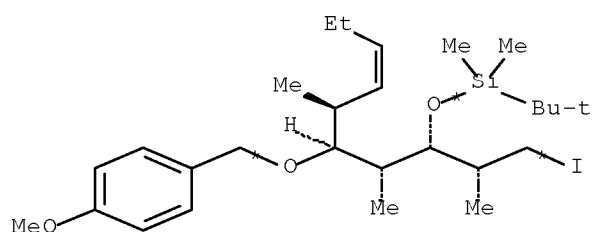
PRO BV 886845-73-4

SOL 7732-18-5 Water, 67-56-1 MeOH

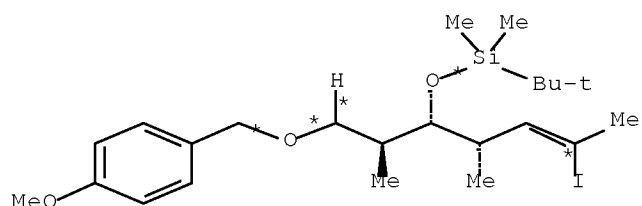
CON 3 hours, room temperature

NTE incremental addition of the reagent

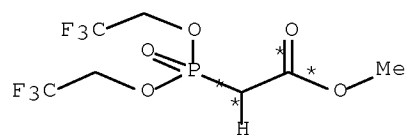
RX(136) OF 136 COMPOSED OF RX(12), RX(13), RX(14), RX(15), RX(16), RX(17),
 RX(9), RX(18), RX(19), RX(26)
 RX(136) AN + AO + BB + H + BF ==> BW



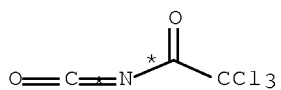
AN



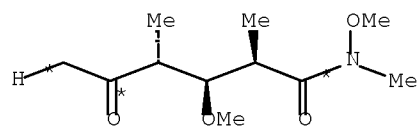
AO



BB

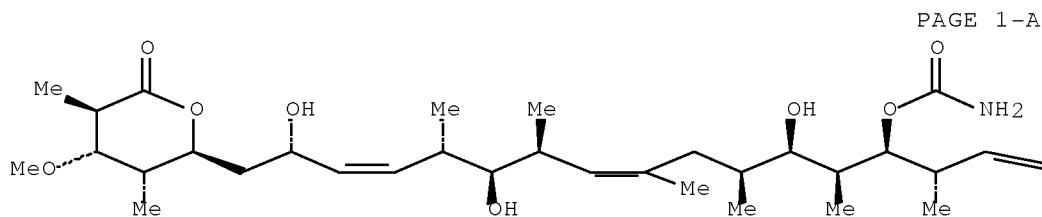


H



BF

10
 STEPS
 →



PAGE 1-B



BW
YIELD 92%

RX(12) RCT AN 870075-02-8

STAGE(1)

RGT AQ 109-72-8 BuLi, AR 7646-85-7 ZnCl₂
 SOL 60-29-7 Et₂O, 109-66-0 Pentane
 CON SUBSTAGE(1) room temperature -> -78 deg C
 SUBSTAGE(2) 5 minutes, -78 deg C
 SUBSTAGE(3) -78 deg C -> room temperature
 SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AO 212703-48-5
 CAT 14221-01-3 Pd(PPh₃)₄
 CON 15 hours, room temperature

STAGE(3)

RGT P 7732-18-5 Water
 CON room temperature

PRO AP 886845-60-9
 NTE in the dark in stage 2

RX(13) RCT AP 886845-60-9

STAGE(1)

RGT AV 84-58-2 DDQ
 SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
 CON 30 minutes, 0 deg C

STAGE(2)

RGT AW 16940-66-2 NaBH₄
 SOL 67-56-1 MeOH
 CON 10 minutes, room temperature

STAGE(3)
 RGT AX 12125-02-9 NH4Cl
 SOL 7732-18-5 Water
 CON room temperature

 PRO AU 886845-61-0

 RX(14) RCT AU 886845-61-0

 STAGE(1)
 RGT AZ 2564-83-2 Me4-piperidoxyl, BA 1321-07-9 Benzoic acid,
 iodo-
 SOL 75-09-2 CH2Cl2
 CON 2.5 hours, room temperature

 STAGE(2)
 RGT AK 7772-98-7 Na2S2O3
 SOL 7732-18-5 Water
 CON room temperature

 PRO AY 886845-62-1

 RX(15) RCT AY 886845-62-1, BB 88738-78-7
 RGT J 584-08-7 K2CO3
 PRO BC 886845-63-2
 CAT 17455-13-9 18-Crown-6
 SOL 108-88-3 PhMe

 RX(16) RCT BC 886845-63-2, H 3019-71-4

 STAGE(1)
 SOL 75-09-2 CH2Cl2
 CON 1 hour, room temperature

 STAGE(2)
 RGT J 584-08-7 K2CO3
 SOL 67-56-1 MeOH
 CON SUBSTAGE(1) room temperature -> 0 deg C
 SUBSTAGE(2) 1 hour, 0 deg C
 SUBSTAGE(3) 1.5 hours, room temperature

 PRO BD 886845-64-3

 RX(17) RCT BD 886845-64-3

 STAGE(1)
 RGT N 1191-15-7 AlH(Bu-i)2
 SOL 75-09-2 CH2Cl2, 110-54-3 Hexane
 CON 25 minutes, -78 deg C

 STAGE(2)
 RGT O 304-59-6 Rochelle salt
 SOL 7732-18-5 Water
 CON SUBSTAGE(1) 0 deg C
 SUBSTAGE(2) 1.5 deg C

 PRO AI 886845-65-4

 RX(9) RCT AI 886845-65-4

STAGE(1)
RGT S 144-55-8 NaHCO₃, R 87413-09-0 Martin's reagent
SOL 75-09-2 CH₂Cl₂
CON 30 minutes, room temperature

STAGE(2)
RGT AK 7772-98-7 Na₂S₂O₃, S 144-55-8 NaHCO₃
SOL 7732-18-5 Water
CON room temperature

PRO AJ 886845-57-4

RX(18) RCT BF 884313-62-6

STAGE(1)
RGT W 112246-73-8 Bicycloheptylborane, X 121-44-8 Et₃N
SOL 60-29-7 Et₂O
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 0 deg C -> -78 deg C

STAGE(2)
RCT AJ 886845-57-4
SOL 60-29-7 Et₂O
CON SUBSTAGE(1) 3 hours, -78 deg C
SUBSTAGE(2) 16 hours, -20 deg C
SUBSTAGE(3) -20 deg C -> 0 deg C

STAGE(3)
RGT L 67-56-1 MeOH
CON 0 deg C

STAGE(4)
RGT Y 7722-84-1 H₂O₂
SOL 7732-18-5 Water
CON 1 hour, room temperature, pH 7

PRO BG 886845-66-5

NTE stereoselective, phosphate buffered solution used in stage 4

RX(19)

STAGE(1)
RGT AB 109704-53-2 Me₄N.(AcO)₃BH, AC 64-19-7 AcOH
SOL 75-05-8 MeCN
CON SUBSTAGE(1) 30 minutes, room temperature
SUBSTAGE(2) room temperature -> -30 deg C

STAGE(2)
RCT BG 886845-66-5
RGT AC 64-19-7 AcOH
SOL 75-05-8 MeCN
CON SUBSTAGE(1) 30 minutes, -30 deg C
SUBSTAGE(2) 1 hour, 0 deg C

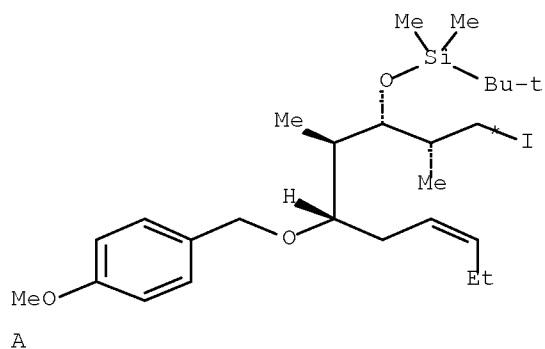
STAGE(3)
RGT O 304-59-6 Rochelle salt
SOL 7732-18-5 Water
CON 5 minutes

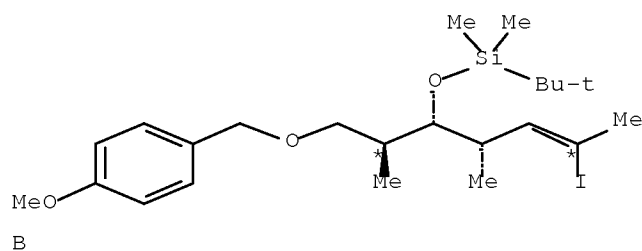
PRO BH 886845-67-6
NTE stereoselective

RX(26) RCT BH 886845-67-6
RGT BT 7647-01-0 HCl
PRO BW 886845-74-5
SOL 7732-18-5 Water, 67-56-1 MeOH
CON 3 hours, room temperature
NTE stereoselective, incremental addition of the reagent

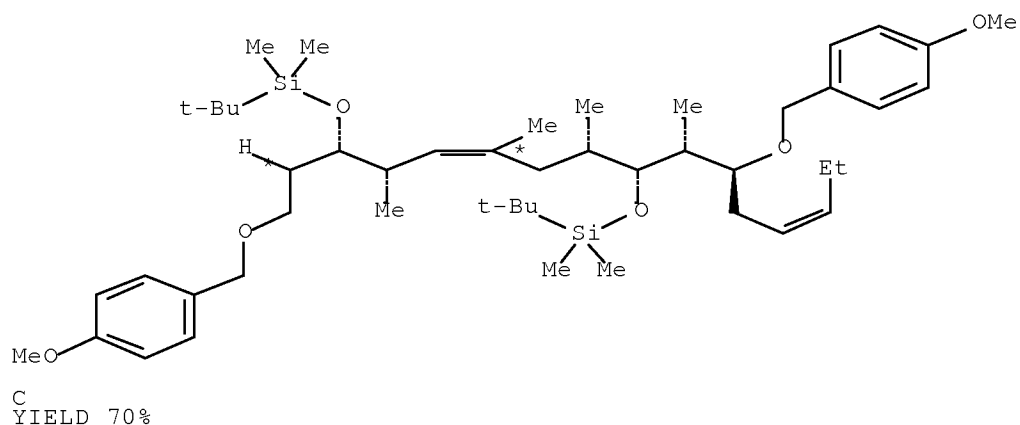
L3 ANSWER 3 OF 9 CASREACT COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 144:412272 CASREACT [Full-text](#)
TITLE: A series of 23,24-dihydrodiscodermolide analogues with
simplified lactone regions
AUTHOR(S): Shaw, Simon J.; Sundermann, Kurt F.; Burlingame, Mark
A.; Zhang, Dan; Petryka, Joseph; Myles, David C.
CORPORATE SOURCE: Kosan Biosciences, Inc., Hayward, CA, 94545, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2006),
16(7), 1961-1964
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A collection of seven new 23,24-dihydrodiscodermolide analogs have been
synthesized with modifications to the lactone ring, some of which show
antiproliferative activities similar to discodermolide.
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(1) OF 119 A + B ==> C...





(1) →



RX(1) RCT A 884313-56-8

STAGE(1)

RGT D 594-19-4 t-BuLi, E 7646-85-7 ZnCl₂

SOL 60-29-7 Et₂O, 109-66-0 Pentane

CON SUBSTAGE(1) 0.83 hours, -78 deg C

SUBSTAGE(2) 1 hour, room temperature

STAGE(2)

RCT B 212703-48-5

CAT 14221-01-3 Pd(PPh₃)₄

CON 15 hours, room temperature

STAGE(3)

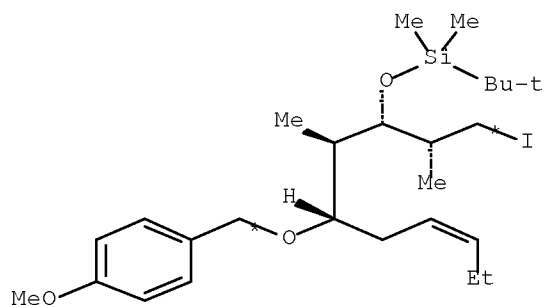
RGT F 7732-18-5 Water

PRO C 884313-57-9

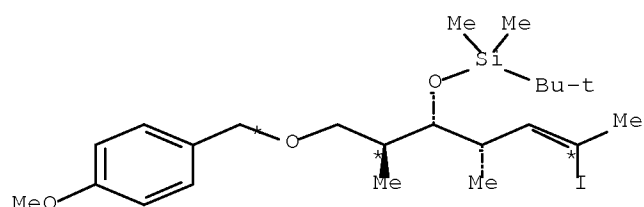
NTE in the dark in stage 2

RX(18) OF 119 COMPOSED OF RX(1), RX(10)

RX(18) A + B ==> AS

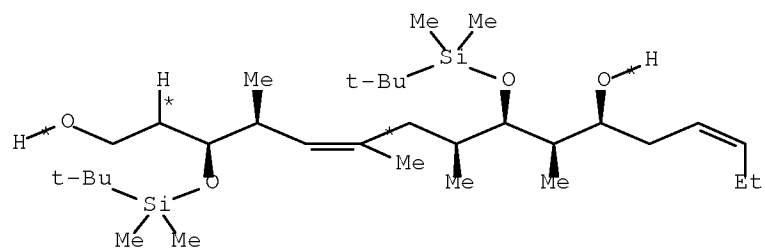


A



B

2
STEPS
→



AS
YIELD 63%

RX(1) RCT A 884313-56-8

STAGE(1)

RGT D 594-19-4 t-BuLi, E 7646-85-7 ZnCl₂
 SOL 60-29-7 Et₂O, 109-66-0 Pentane
 CON SUBSTAGE(1) 0.83 hours, -78 deg C
 SUBSTAGE(2) 1 hour, room temperature

STAGE(2)

RCT B 212703-48-5
 CAT 14221-01-3 Pd(PPh₃)₄
 CON 15 hours, room temperature

STAGE(3)

RGT F 7732-18-5 Water

PRO C 884313-57-9

NTE in the dark in stage 2

RX(10) RCT C 884313-57-9

STAGE(1)

RGT AT 84-58-2 DDQ

SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂

CON 30 minutes, 0 deg C

STAGE(2)

RGT AU 16940-66-2 NaBH₄

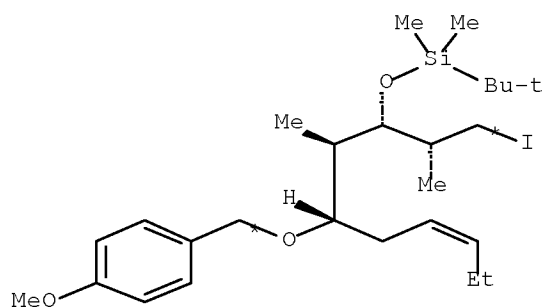
SOL 67-56-1 MeOH

CON 10 minutes

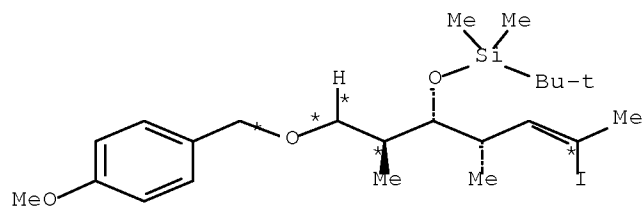
PRO AS 884313-71-7

RX(31) OF 119 COMPOSED OF RX(1), RX(10), RX(11)

RX(31) A + B ==> AV

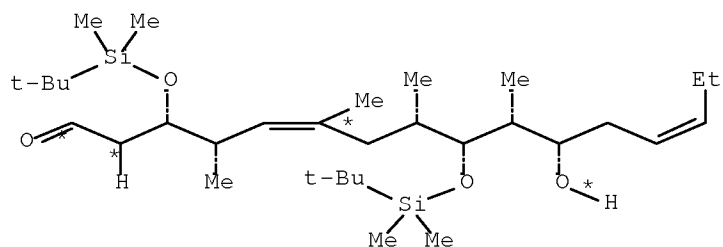


A



B

3
STEPS
→



AV
YIELD 77%

RX(1) RCT A 884313-56-8

STAGE(1)

RGT D 594-19-4 t-BuLi, E 7646-85-7 ZnCl2

SOL 60-29-7 Et2O, 109-66-0 Pentane

CON SUBSTAGE(1) 0.83 hours, -78 deg C

SUBSTAGE(2) 1 hour, room temperature

STAGE(2)

RCT B 212703-48-5

CAT 14221-01-3 Pd(PPh3)4

CON 15 hours, room temperature

STAGE(3)

RGT F 7732-18-5 Water

PRO C 884313-57-9

NTE in the dark in stage 2

RX(10) RCT C 884313-57-9

STAGE(1)

RGT AT 84-58-2 DDQ

SOL 7732-18-5 Water, 75-09-2 CH2Cl2

CON 30 minutes, 0 deg C

STAGE(2)

RGT AU 16940-66-2 NaBH4

SOL 67-56-1 MeOH

CON 10 minutes

PRO AS 884313-71-7

RX(11) RCT AS 884313-71-7

STAGE(1)

RGT AW 2564-83-2 Me4-piperidoxyl, AX 88-67-5 Benzoic acid,
2-iodo-

SOL 75-09-2 CH2Cl2

CON 2.5 hours, room temperature

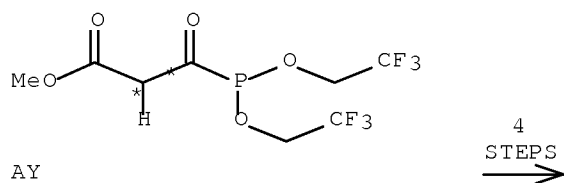
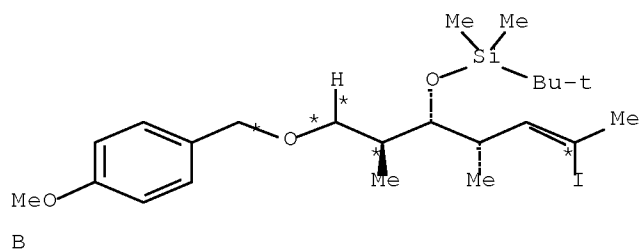
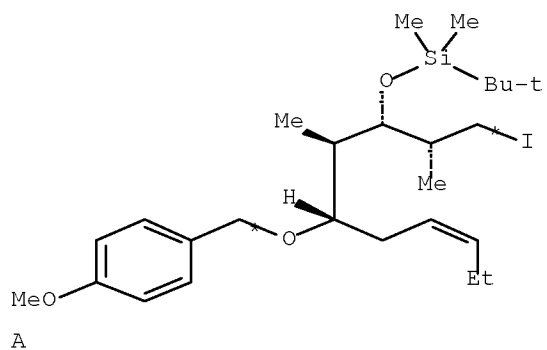
STAGE(2)

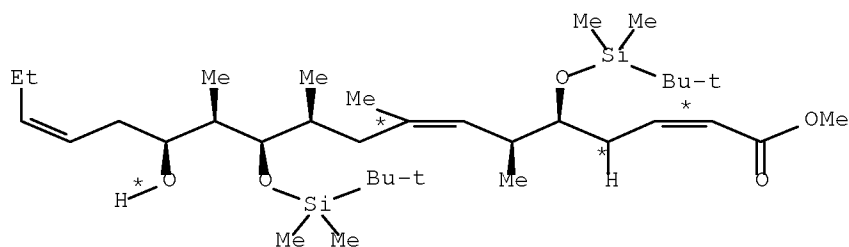
RGT N 7772-98-7 Na2S2O3

SOL 7732-18-5 Water

PRO AV 884313-72-8
 NTE chemoselective, regioselective

RX(41) OF 119 COMPOSED OF RX(1), RX(10), RX(11), RX(12)
 RX(41) A + B + AY ==> AZ





AZ
YIELD 81%

RX(1) RCT A 884313-56-8

STAGE(1)

RGT D 594-19-4 t-BuLi, E 7646-85-7 ZnCl₂

SOL 60-29-7 Et₂O, 109-66-0 Pentane

CON SUBSTAGE(1) 0.83 hours, -78 deg C

SUBSTAGE(2) 1 hour, room temperature

STAGE(2)

RCT B 212703-48-5

CAT 14221-01-3 Pd(PPh₃)₄

CON 15 hours, room temperature

STAGE(3)

RGT F 7732-18-5 Water

PRO C 884313-57-9

NTE in the dark in stage 2

RX(10) RCT C 884313-57-9

STAGE(1)

RGT AT 84-58-2 DDQ

SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂

CON 30 minutes, 0 deg C

STAGE(2)

RGT AU 16940-66-2 NaBH₄

SOL 67-56-1 MeOH

CON 10 minutes

PRO AS 884313-71-7

RX(11) RCT AS 884313-71-7

STAGE(1)

RGT AW 2564-83-2 Me₄-piperidoxyl, AX 88-67-5 Benzoic acid,
2-iodo-

SOL 75-09-2 CH₂Cl₂

CON 2.5 hours, room temperature

STAGE(2)

RGT N 7772-98-7 Na₂S₂O₃

SOL 7732-18-5 Water

PRO AV 884313-72-8
NTE chemoselective, regioselective

RX(12)

STAGE(1)

RGT BA 584-08-7 K2CO3, BB 17455-13-9 18-Crown-6
SOL 108-88-3 PhMe
CON 1 hour, room temperature

STAGE(2)

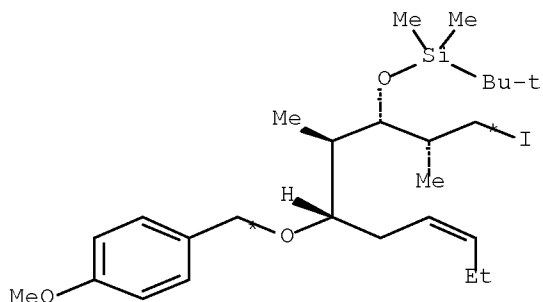
RCT AV 884313-72-8, AY 884313-77-3
SOL 108-88-3 PhMe
CON SUBSTAGE(1) 1 hour, -20 deg C
SUBSTAGE(2) 2 hours, 0 deg C

PRO AZ 884313-73-9

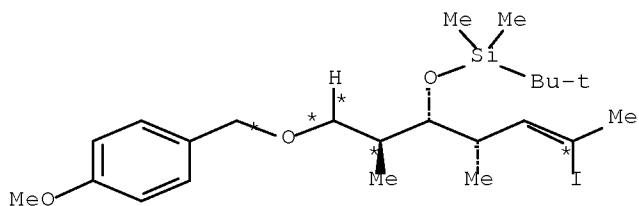
NTE stereoselective, Still-Gennari reaction

RX(55) OF 119 COMPOSED OF RX(1), RX(10), RX(11), RX(12), RX(13)

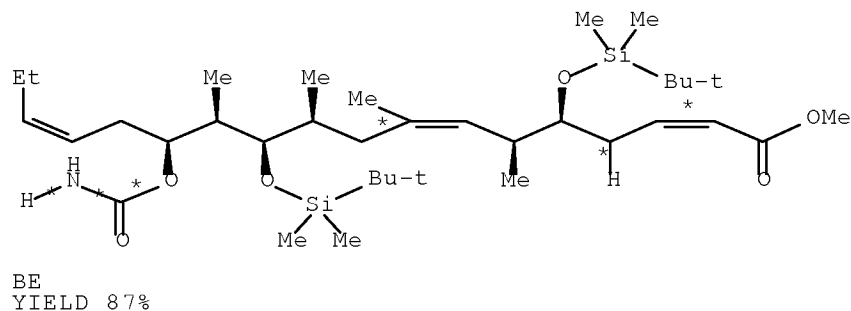
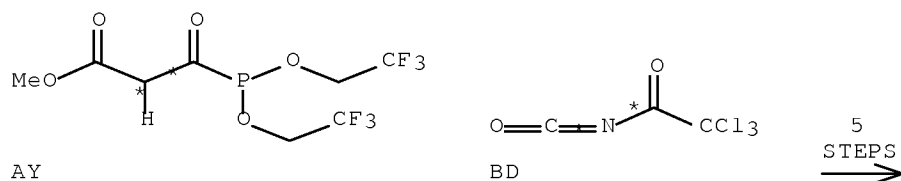
RX(55) A + B + AY + BD ==> BE



A



B



RX(1) RCT A 884313-56-8

STAGE(1)

RGT D 594-19-4 t-BuLi, E 7646-85-7 ZnCl₂
 SOL 60-29-7 Et₂O, 109-66-0 Pentane
 CON SUBSTAGE(1) 0.83 hours, -78 deg C
 SUBSTAGE(2) 1 hour, room temperature

STAGE(2)

RCT B 212703-48-5
 CAT 14221-01-3 Pd(PPh₃)₄
 CON 15 hours, room temperature

STAGE(3)

RGT F 7732-18-5 Water

PRO C 884313-57-9

NTE in the dark in stage 2

RX(10) RCT C 884313-57-9

STAGE(1)

RGT AT 84-58-2 DDQ
 SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
 CON 30 minutes, 0 deg C

STAGE(2)

RGT AU 16940-66-2 NaBH₄
 SOL 67-56-1 MeOH
 CON 10 minutes

PRO AS 884313-71-7

RX(11) RCT AS 884313-71-7

STAGE(1)
RGT AW 2564-83-2 Me4-piperidoxyl, AX 88-67-5 Benzoic acid,
2-iodo-
SOL 75-09-2 CH2Cl2
CON 2.5 hours, room temperature

STAGE(2)
RGT N 7772-98-7 Na2S2O3
SOL 7732-18-5 Water

PRO AV 884313-72-8
NTE chemoselective, regioselective

RX(12)

STAGE(1)
RGT BA 584-08-7 K2CO3, BB 17455-13-9 18-Crown-6
SOL 108-88-3 PhMe
CON 1 hour, room temperature

STAGE(2)
RCT AV 884313-72-8, AY 884313-77-3
SOL 108-88-3 PhMe
CON SUBSTAGE(1) 1 hour, -20 deg C
SUBSTAGE(2) 2 hours, 0 deg C

PRO AZ 884313-73-9
NTE stereoselective, Still-Gennari reaction

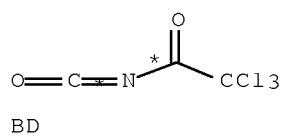
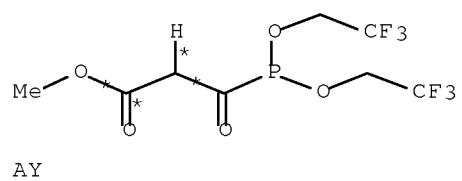
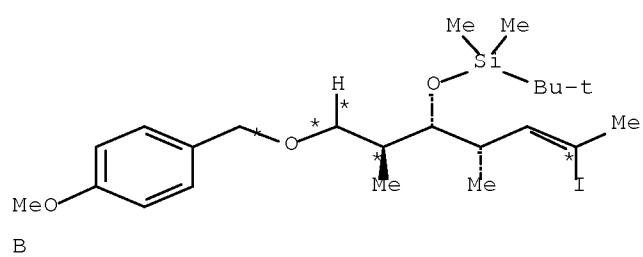
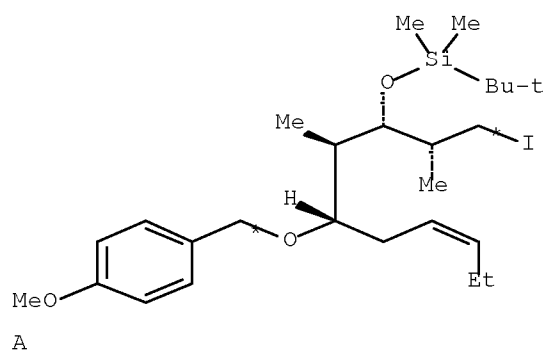
RX(13) RCT AZ 884313-73-9, BD 3019-71-4

STAGE(1)
SOL 75-09-2 CH2Cl2
CON 1 hour, room temperature

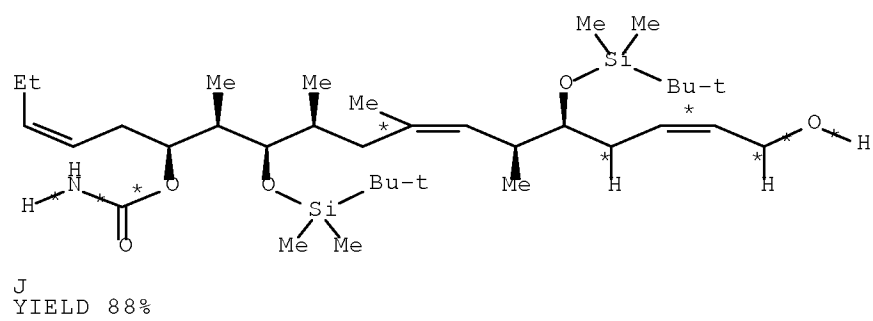
STAGE(2)
RGT BA 584-08-7 K2CO3
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 1.5 hours, room temperature

PRO BE 884313-74-0

RX(78) OF 119 COMPOSED OF RX(1), RX(10), RX(11), RX(12), RX(13), RX(14)
RX(78) A + B + AY + BD ==> J



6
STEPS
→



STAGE(1)
RGT D 594-19-4 t-BuLi, E 7646-85-7 ZnCl2
SOL 60-29-7 Et2O, 109-66-0 Pentane
CON SUBSTAGE(1) 0.83 hours, -78 deg C
SUBSTAGE(2) 1 hour, room temperature

STAGE(2)
RCT B 212703-48-5
CAT 14221-01-3 Pd(PPh3)4
CON 15 hours, room temperature

STAGE(3)
RGT F 7732-18-5 Water

PRO C 884313-57-9
NTE in the dark in stage 2

RX(10) RCT C 884313-57-9

STAGE(1)
RGT AT 84-58-2 DDQ
SOL 7732-18-5 Water, 75-09-2 CH2Cl2
CON 30 minutes, 0 deg C

STAGE(2)
RGT AU 16940-66-2 NaBH4
SOL 67-56-1 MeOH
CON 10 minutes

PRO AS 884313-71-7

RX(11) RCT AS 884313-71-7

STAGE(1)
RGT AW 2564-83-2 Me4-piperidoxyl, AX 88-67-5 Benzoic acid,
2-iodo-
SOL 75-09-2 CH2Cl2
CON 2.5 hours, room temperature

STAGE(2)
RGT N 7772-98-7 Na2S2O3
SOL 7732-18-5 Water

PRO AV 884313-72-8
NTE chemoselective, regioselective

RX(12)

STAGE(1)
RGT BA 584-08-7 K2CO3, BB 17455-13-9 18-Crown-6
SOL 108-88-3 PhMe
CON 1 hour, room temperature

STAGE(2)
RCT AV 884313-72-8, AY 884313-77-3
SOL 108-88-3 PhMe
CON SUBSTAGE(1) 1 hour, -20 deg C
SUBSTAGE(2) 2 hours, 0 deg C

RX(13) RCT AZ 884313-73-9, BD 3019-71-4

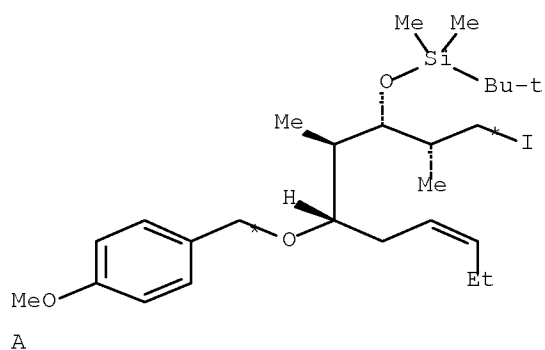
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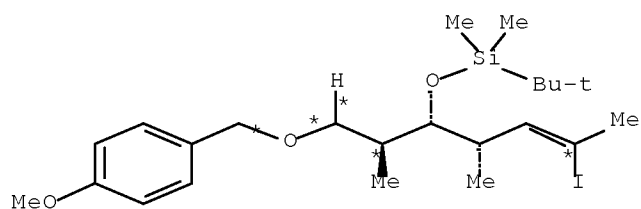
STAGE(2)
  RGT  BA 584-08-7 K2CO3
  SOL  67-56-1 MeOH
  CON  SUBSTAGE(1) 1 hour, 0 deg C
        SUBSTAGE(2) 1.5 hours, room temperature

```

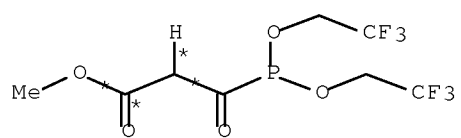
RX(14) RCT BE 884313-74-0

STAGE(2)
RGT BG 304-59-6 Rochelle salt
SOL 7732-18-5 Water
CON 1.5 hours, 0 deg C

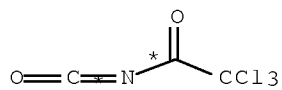
$$\begin{array}{l} \text{RX(81) OF 119 COMPOSED OF RX(1), RX(10), RX(11), RX(12), RX(13), RX(14), RX(2)} \\ \text{RX(81) \quad A \quad + \quad B \quad + \quad AY \quad + \quad BD \quad ==> \quad K} \end{array}$$




B

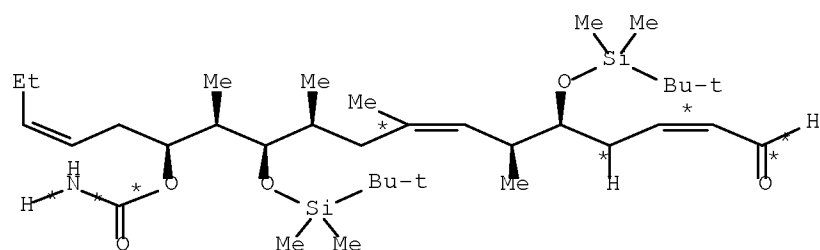


AY



BD

7
STEPS
➔



K
YIELD 87%

RX(1) RCT A 884313-56-8

STAGE(1)

RGT D 594-19-4 t-BuLi, E 7646-85-7 ZnCl₂
SOL 60-29-7 Et₂O, 109-66-0 Pentane
CON SUBSTAGE(1) 0.83 hours, -78 deg C
SUBSTAGE(2) 1 hour, room temperature

STAGE(2)

RCT B 212703-48-5
CAT 14221-01-3 Pd(PPh₃)₄
CON 15 hours, room temperature

STAGE(3)

RGT F 7732-18-5 Water

PRO C 884313-57-9

NTE in the dark in stage 2

RX(10) RCT C 884313-57-9

STAGE(1)

RGT AT 84-58-2 DDQ
SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
CON 30 minutes, 0 deg C

STAGE(2)

RGT AU 16940-66-2 NaBH₄
SOL 67-56-1 MeOH
CON 10 minutes

PRO AS 884313-71-7

RX(11) RCT AS 884313-71-7

STAGE(1)

RGT AW 2564-83-2 Me₄-piperidoxyl, AX 88-67-5 Benzoic acid,
2-iodo-
SOL 75-09-2 CH₂Cl₂
CON 2.5 hours, room temperature

STAGE(2)

RGT N 7772-98-7 Na₂S₂O₃
SOL 7732-18-5 Water

PRO AV 884313-72-8

NTE chemoselective, regioselective

RX(12)

STAGE(1)

RGT BA 584-08-7 K₂CO₃, BB 17455-13-9 18-Crown-6
SOL 108-88-3 PhMe
CON 1 hour, room temperature

STAGE(2)

RCT AV 884313-72-8, AY 884313-77-3
SOL 108-88-3 PhMe
CON SUBSTAGE(1) 1 hour, -20 deg C
SUBSTAGE(2) 2 hours, 0 deg C

PRO AZ 884313-73-9

NTE stereoselective, Still-Gennari reaction

RX(13) RCT AZ 884313-73-9, BD 3019-71-4

STAGE(1)

SOL 75-09-2 CH₂Cl₂
CON 1 hour, room temperature

STAGE(2)

RGT BA 584-08-7 K₂CO₃
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 1.5 hours, room temperature

PRO BE 884313-74-0

RX(14) RCT BE 884313-74-0

STAGE(1)

RGT BF 1191-15-7 $\text{AlH}(\text{Bu-i})_2$
SOL 75-09-2 CH_2Cl_2 , 110-54-3 Hexane
CON 25 minutes, -78 deg C

STAGE(2)

RGT BG 304-59-6 Rochelle salt
SOL 7732-18-5 Water
CON 1.5 hours, 0 deg C

PRO J 884313-75-1

RX(2) RCT J 884313-75-1

STAGE(1)

RGT L 144-55-8 NaHCO_3 , M 87413-09-0 Martin's reagent
SOL 75-09-2 CH_2Cl_2
CON 30 minutes, room temperature

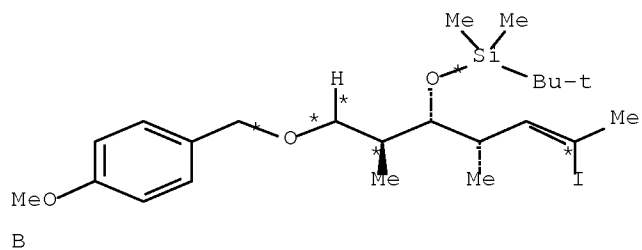
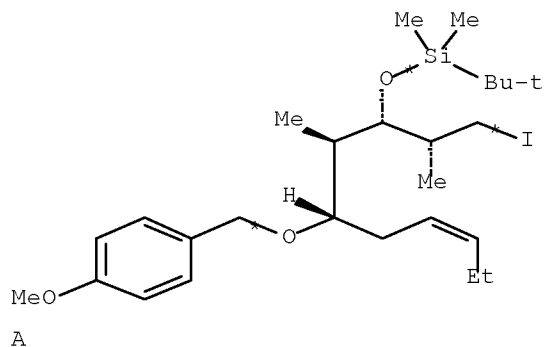
STAGE(2)

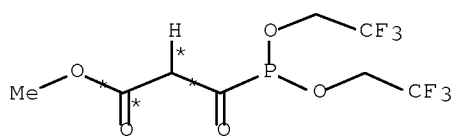
RGT N 7772-98-7 $\text{Na}_2\text{S}_2\text{O}_3$, L 144-55-8 NaHCO_3
SOL 7732-18-5 Water

PRO K 884313-58-0

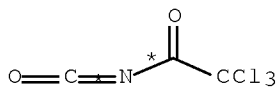
RX(88) OF 119 COMPOSED OF RX(1), RX(10), RX(11), RX(12), RX(13), RX(14), RX(2),
RX(3)

RX(88) A + B + AY + BD + P ==> Q

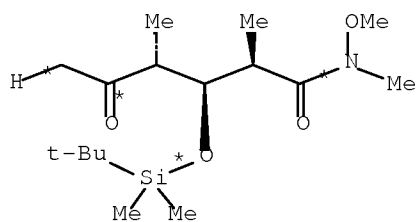




AY

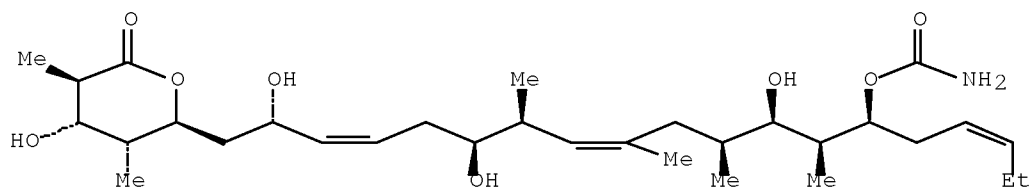


BD



P

8
STEPS
➔



Q

RX(1) RCT A 884313-56-8

STAGE(1)

RGT D 594-19-4 t-BuLi, E 7646-85-7 ZnCl2

SOL 60-29-7 Et2O, 109-66-0 Pentane

CON SUBSTAGE(1) 0.83 hours, -78 deg C

SUBSTAGE(2) 1 hour, room temperature

STAGE(2)

RCT B 212703-48-5

CAT 14221-01-3 Pd(PPh3)4

CON 15 hours, room temperature

STAGE(3)

RGT F 7732-18-5 Water

PRO C 884313-57-9
NTE in the dark in stage 2

RX(10) RCT C 884313-57-9

STAGE(1)
RGT AT 84-58-2 DDQ
SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
CON 30 minutes, 0 deg C

STAGE(2)
RGT AU 16940-66-2 NaBH₄
SOL 67-56-1 MeOH
CON 10 minutes

PRO AS 884313-71-7

RX(11) RCT AS 884313-71-7

STAGE(1)
RGT AW 2564-83-2 Me₄-piperidoxyl, AX 88-67-5 Benzoic acid,
2-iodo-
SOL 75-09-2 CH₂Cl₂
CON 2.5 hours, room temperature

STAGE(2)
RGT N 7772-98-7 Na₂S₂O₃
SOL 7732-18-5 Water

PRO AV 884313-72-8
NTE chemoselective, regioselective

RX(12)

STAGE(1)
RGT BA 584-08-7 K₂CO₃, BB 17455-13-9 18-Crown-6
SOL 108-88-3 PhMe
CON 1 hour, room temperature

STAGE(2)
RCT AV 884313-72-8, AY 884313-77-3
SOL 108-88-3 PhMe
CON SUBSTAGE(1) 1 hour, -20 deg C
SUBSTAGE(2) 2 hours, 0 deg C

PRO AZ 884313-73-9
NTE stereoselective, Still-Gennari reaction

RX(13) RCT AZ 884313-73-9, BD 3019-71-4

STAGE(1)
SOL 75-09-2 CH₂Cl₂
CON 1 hour, room temperature

STAGE(2)
RGT BA 584-08-7 K₂CO₃
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 1.5 hours, room temperature

PRO BE 884313-74-0

RX(14) RCT BE 884313-74-0

STAGE(1)

RGT BF 1191-15-7 AlH(Bu-i)2
SOL 75-09-2 CH2Cl2, 110-54-3 Hexane
CON 25 minutes, -78 deg C

STAGE(2)

RGT BG 304-59-6 Rochelle salt
SOL 7732-18-5 Water
CON 1.5 hours, 0 deg C

PRO J 884313-75-1

RX(2) RCT J 884313-75-1

STAGE(1)

RGT L 144-55-8 NaHCO3, M 87413-09-0 Martin's reagent
SOL 75-09-2 CH2Cl2
CON 30 minutes, room temperature

STAGE(2)

RGT N 7772-98-7 Na2S2O3, L 144-55-8 NaHCO3
SOL 7732-18-5 Water

PRO K 884313-58-0

RX(3) RCT K 884313-58-0, P 397331-43-0

STAGE(1)

RGT R 112246-73-8 Bicycloheptylborane, S 121-44-8 Et3N
SOL 60-29-7 Et2O

STAGE(2)

RGT T 56553-60-7 Na.(AcO)3BH

STAGE(3)

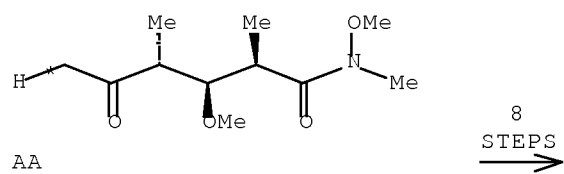
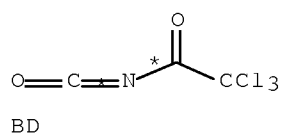
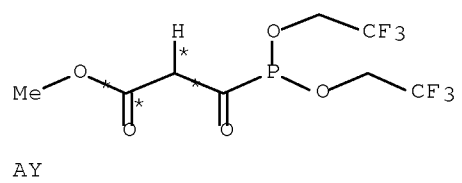
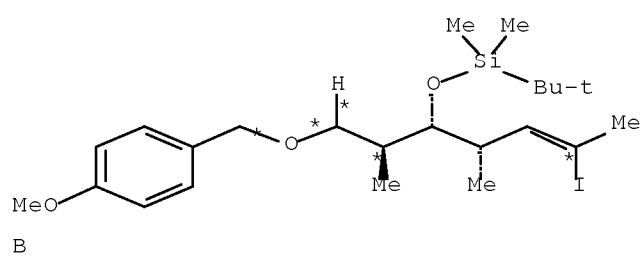
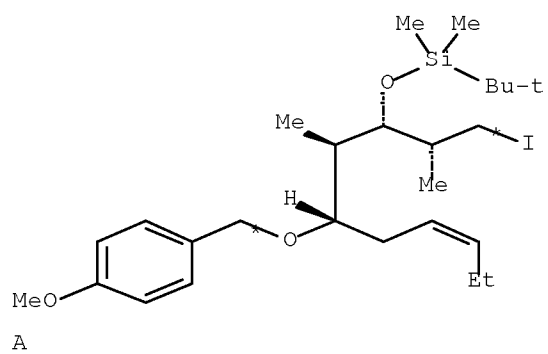
RGT U 7647-01-0 HCl
SOL 67-56-1 MeOH

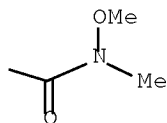
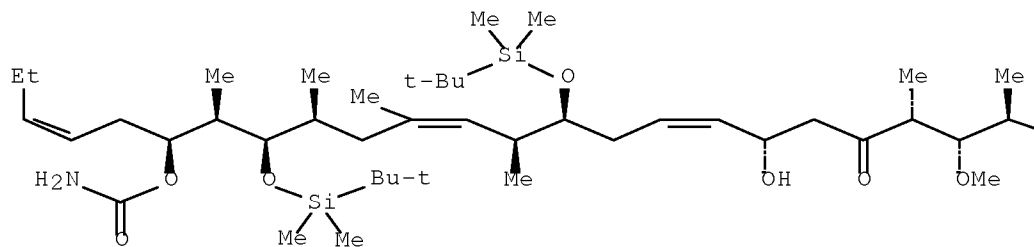
PRO Q 884313-59-1

NTE stereoselective

RX(89) OF 119 COMPOSED OF RX(1), RX(10), RX(11), RX(12), RX(13), RX(14), RX(2),
RX(15)

RX(89) A + B + AY + BD + AA ==> EI





BI
YIELD 87%

RX(1) RCT A 884313-56-8

STAGE(1)

RGT D 594-19-4 t-BuLi, E 7646-85-7 ZnCl2

SOL 60-29-7 Et2O, 109-66-0 Pentane

CON SUBSTAGE(1) 0.83 hours, -78 deg C

SUBSTAGE(2) 1 hour, room temperature

STAGE(2)

RCT B 212703-48-5

CAT 14221-01-3 Pd(PPh3)4

CON 15 hours, room temperature

STAGE(3)

RGT F 7732-18-5 Water

PRO C 884313-57-9

NTE in the dark in stage 2

RX(10) RCT C 884313-57-9

STAGE(1)

RGT AT 84-58-2 DDQ

SOL 7732-18-5 Water, 75-09-2 CH2Cl2

CON 30 minutes, 0 deg C

STAGE(2)

RGT AU 16940-66-2 NaBH4

SOL 67-56-1 MeOH

CON 10 minutes

PRO AS 884313-71-7

RX(11) RCT AS 884313-71-7

STAGE(1)

RGT AW 2564-83-2 Me4-piperidoxyl, AX 88-67-5 Benzoic acid,
2-iodo-

SOL 75-09-2 CH₂Cl₂

CON 2.5 hours, room temperature

STAGE(2)

RGT N 7772-98-7 Na₂S₂O₃

SOL 7732-18-5 Water

PRO AV 884313-72-8

NTE chemoselective, regioselective

RX(12)

STAGE(1)

RGT BA 584-08-7 K₂CO₃, BB 17455-13-9 18-Crown-6

SOL 108-88-3 PhMe

CON 1 hour, room temperature

STAGE(2)

RCT AV 884313-72-8, AY 884313-77-3

SOL 108-88-3 PhMe

CON SUBSTAGE(1) 1 hour, -20 deg C

SUBSTAGE(2) 2 hours, 0 deg C

PRO AZ 884313-73-9

NTE stereoselective, Still-Gennari reaction

RX(13) RCT AZ 884313-73-9, BD 3019-71-4

STAGE(1)

SOL 75-09-2 CH₂Cl₂

CON 1 hour, room temperature

STAGE(2)

RGT BA 584-08-7 K₂CO₃

SOL 67-56-1 MeOH

CON SUBSTAGE(1) 1 hour, 0 deg C

SUBSTAGE(2) 1.5 hours, room temperature

PRO BE 884313-74-0

RX(14) RCT BE 884313-74-0

STAGE(1)

RGT BF 1191-15-7 AlH(Bu-i)₂

SOL 75-09-2 CH₂Cl₂, 110-54-3 Hexane

CON 25 minutes, -78 deg C

STAGE(2)

RGT BG 304-59-6 Rochelle salt

SOL 7732-18-5 Water

CON 1.5 hours, 0 deg C

PRO J 884313-75-1

RX(2) RCT J 884313-75-1

STAGE(1)

RGT L 144-55-8 NaHCO₃, M 87413-09-0 Martin's reagent

SOL 75-09-2 CH₂Cl₂

CON 30 minutes, room temperature

STAGE(2)

RGT N 7772-98-7 Na₂S₂O₃, L 144-55-8 NaHCO₃

SOL 7732-18-5 Water

PRO K 884313-58-0

RX(15) RCT AA 884313-62-6

STAGE(1)

RGT R 112246-73-8 Bicycloheptylborane, S 121-44-8 Et₃N

SOL 60-29-7 Et₂O

CON 1 hour, 0 deg C

STAGE(2)

RCT K 884313-58-0

SOL 60-29-7 Et₂O

CON SUBSTAGE(1) 3 hours, -78 deg C

SUBSTAGE(2) 16 hours, -20 deg C

STAGE(3)

RGT BJ 7722-84-1 H₂O₂

SOL 7732-18-5 Water, 67-56-1 MeOH

CON SUBSTAGE(1) 0 deg C, pH 7

SUBSTAGE(2) 1 hour, room temperature

PRO BI 884313-76-2

NTE stereoselective, buffered soln. in stage 3

VERIFICATION INCOMPLETE - REACTION MAP DATA UNAVAILABLE

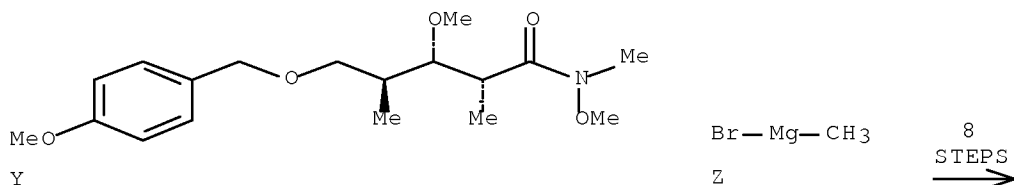
RX(99) OF 119 COMPOSED OF REACTION SEQUENCE RX(5), RX(15)

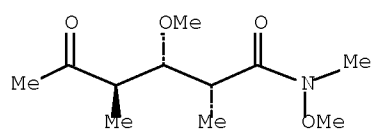
AND REACTION SEQUENCE RX(1), RX(10), RX(11), RX(12), RX(13),

RX(14), RX(2), RX(15)

...Y + Z ==> AA...

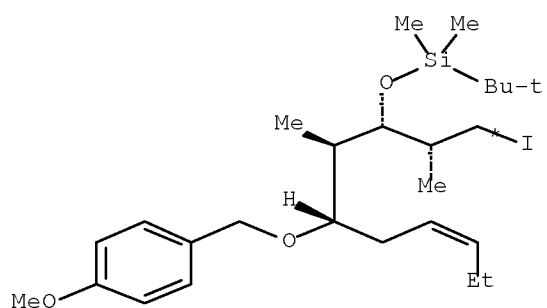
... A + E + AY + BD + AA ==> BI



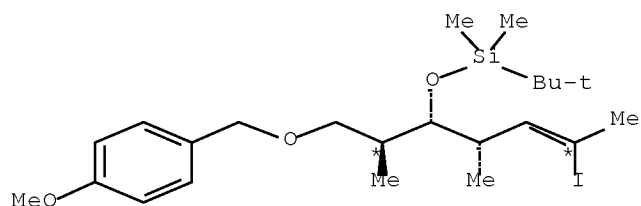


AA

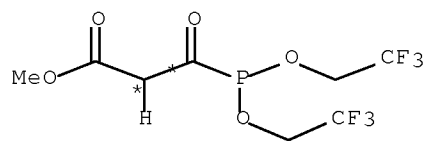
START NEXT REACTION SEQUENCE



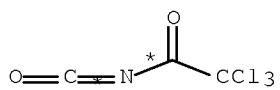
A



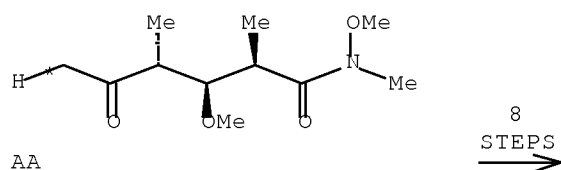
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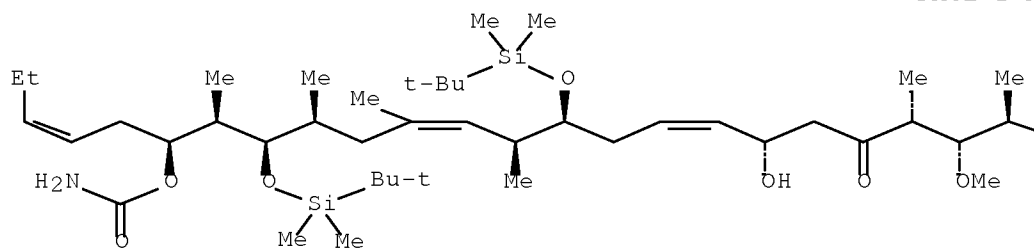
AY



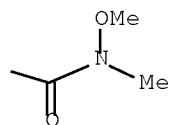
BD



PAGE 1-A



PAGE 1-B



BI
YIELD 87%

RX(5) RCT Y 884313-70-6

STAGE(1)

RGT AB 1333-74-0 H2

CAT 12135-22-7 Pd(OH)2

STAGE(2)

RGT AC 67-68-5 DMSO, S 121-44-8 Et3N, AD 79-37-8 (COCl)2

STAGE(3)

RCT Z 75-16-1

PRO AA 884313-62-6

RX(1) RCT A 884313-56-8

STAGE(1)

RGT D 594-19-4 t-BuLi, E 7646-85-7 ZnCl2
SOL 60-29-7 Et2O, 109-66-0 Pentane
CON SUBSTAGE(1) 0.83 hours, -78 deg C
SUBSTAGE(2) 1 hour, room temperature

STAGE(2)
RCT B 212703-48-5
CAT 14221-01-3 Pd(PPh3)4
CON 15 hours, room temperature

STAGE(3)
RGT F 7732-18-5 Water

PRO C 884313-57-9
NTE in the dark in stage 2

RX(10) RCT C 884313-57-9

STAGE(1)
RGT AT 84-58-2 DDQ
SOL 7732-18-5 Water, 75-09-2 CH2Cl2
CON 30 minutes, 0 deg C

STAGE(2)
RGT AU 16940-66-2 NaBH4
SOL 67-56-1 MeOH
CON 10 minutes

PRO AS 884313-71-7

RX(11) RCT AS 884313-71-7

STAGE(1)
RGT AW 2564-83-2 Me4-piperidoxyl, AX 88-67-5 Benzoic acid,
2-iodo-
SOL 75-09-2 CH2Cl2
CON 2.5 hours, room temperature

STAGE(2)
RGT N 7772-98-7 Na2S2O3
SOL 7732-18-5 Water

PRO AV 884313-72-8
NTE chemoselective, regioselective

RX(12)

STAGE(1)
RGT BA 584-08-7 K2CO3, BB 17455-13-9 18-Crown-6
SOL 108-88-3 PhMe
CON 1 hour, room temperature

STAGE(2)
RCT AV 884313-72-8, AY 884313-77-3
SOL 108-88-3 PhMe
CON SUBSTAGE(1) 1 hour, -20 deg C
SUBSTAGE(2) 2 hours, 0 deg C

PRO AZ 884313-73-9
NTE stereoselective, Still-Gennari reaction

RX(13) RCT AZ 884313-73-9, BD 3019-71-4

STAGE(1)
SOL 75-09-2 CH₂Cl₂
CON 1 hour, room temperature

STAGE(2)
RGT BA 584-08-7 K₂CO₃
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 1.5 hours, room temperature

PRO BE 884313-74-0

RX(14) RCT BE 884313-74-0

STAGE(1)
RGT BF 1191-15-7 AlH(Bu-i)₂
SOL 75-09-2 CH₂Cl₂, 110-54-3 Hexane
CON 25 minutes, -78 deg C

STAGE(2)
RGT BG 304-59-6 Rochelle salt
SOL 7732-18-5 Water
CON 1.5 hours, 0 deg C

PRO J 884313-75-1

RX(2) RCT J 884313-75-1

STAGE(1)
RGT L 144-55-8 NaHCO₃, M 87413-09-0 Martin's reagent
SOL 75-09-2 CH₂Cl₂
CON 30 minutes, room temperature

STAGE(2)
RGT N 7772-98-7 Na₂S₂O₃, L 144-55-8 NaHCO₃
SOL 7732-18-5 Water

PRO K 884313-58-0

RX(15) RCT AA 884313-62-6

STAGE(1)
RGT R 112246-73-8 Bicycloheptylborane, S 121-44-8 Et₃N
SOL 60-29-7 Et₂O
CON 1 hour, 0 deg C

STAGE(2)
RCT K 884313-58-0
SOL 60-29-7 Et₂O
CON SUBSTAGE(1) 3 hours, -78 deg C
SUBSTAGE(2) 16 hours, -20 deg C

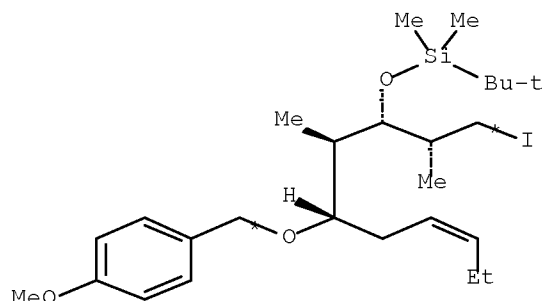
STAGE(3)
RGT BJ 7722-84-1 H₂O₂
SOL 7732-18-5 Water, 67-56-1 MeOH
CON SUBSTAGE(1) 0 deg C, pH 7
SUBSTAGE(2) 1 hour, room temperature

PRO BI 884313-76-2

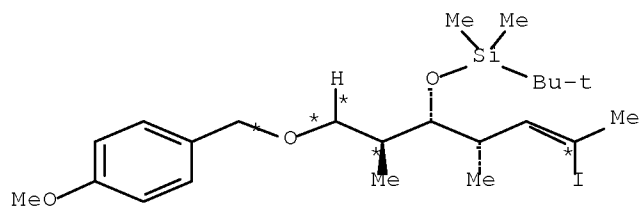
NTE stereoselective, buffered soln. in stage 3

RX(100) OF 119 COMPOSED OF RX(1), RX(10), RX(11), RX(12), RX(13), RX(14),
RX(2), RX(15), RX(16)

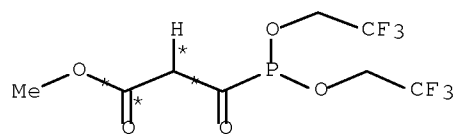
RX(100) A + E + AY + BD + AA ==> W



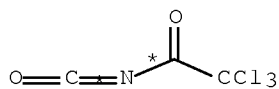
A



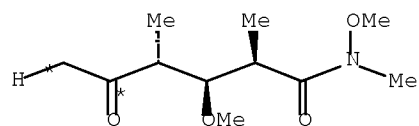
B



AY



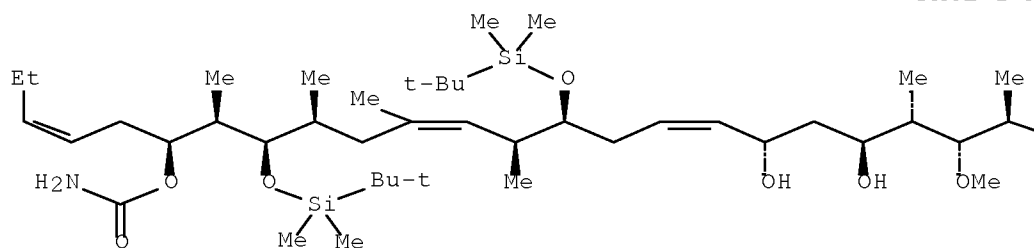
BD



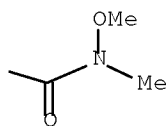
AA

9
STEPS
→

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PAGE 1-B



W
YIELD 81%

RX(1) RCT A 884313-56-8

STAGE(1)

RGT D 594-19-4 t-BuLi, E 7646-85-7 ZnCl2

SOL 60-29-7 Et2O, 109-66-0 Pentane

CON SUBSTAGE(1) 0.83 hours, -78 deg C

SUBSTAGE(2) 1 hour, room temperature

STAGE(2)

RCT B 212703-48-5

CAT 14221-01-3 Pd(PPh3)4

CON 15 hours, room temperature

STAGE(3)

RGT F 7732-18-5 Water

PRO C 884313-57-9

NTE in the dark in stage 2

RX(10) RCT C 884313-57-9

STAGE(1)

RGT AT 84-58-2 DDQ

SOL 7732-18-5 Water, 75-09-2 CH2Cl2

CON 30 minutes, 0 deg C

STAGE(2)
 RGT AU 16940-66-2 NaBH4
 SOL 67-56-1 MeOH
 CON 10 minutes

 PRO AS 884313-71-7

 RX(11) RCT AS 884313-71-7

 STAGE(1)
 RGT AW 2564-83-2 Me4-piperidoxyl, AX 88-67-5 Benzoic acid,
 2-iodo-
 SOL 75-09-2 CH2Cl2
 CON 2.5 hours, room temperature

 STAGE(2)
 RGT N 7772-98-7 Na2S2O3
 SOL 7732-18-5 Water

 PRO AV 884313-72-8
 NTE chemoselective, regioselective

 RX(12)

 STAGE(1)
 RGT BA 584-08-7 K2CO3, BB 17455-13-9 18-Crown-6
 SOL 108-88-3 PhMe
 CON 1 hour, room temperature

 STAGE(2)
 RCT AV 884313-72-8, AY 884313-77-3
 SOL 108-88-3 PhMe
 CON SUBSTAGE(1) 1 hour, -20 deg C
 SUBSTAGE(2) 2 hours, 0 deg C

 PRO AZ 884313-73-9
 NTE stereoselective, Still-Gennari reaction

 RX(13) RCT AZ 884313-73-9, BD 3019-71-4

 STAGE(1)
 SOL 75-09-2 CH2Cl2
 CON 1 hour, room temperature

 STAGE(2)
 RGT BA 584-08-7 K2CO3
 SOL 67-56-1 MeOH
 CON SUBSTAGE(1) 1 hour, 0 deg C
 SUBSTAGE(2) 1.5 hours, room temperature

 PRO BE 884313-74-0

 RX(14) RCT BE 884313-74-0

 STAGE(1)
 RGT BF 1191-15-7 AlH(Bu-i)2
 SOL 75-09-2 CH2Cl2, 110-54-3 Hexane
 CON 25 minutes, -78 deg C

STAGE(2)
RGT BG 304-59-6 Rochelle salt
SOL 7732-18-5 Water
CON 1.5 hours, 0 deg C

PRO J 884313-75-1

RX(2) RCT J 884313-75-1

STAGE(1)
RGT L 144-55-8 NaHCO₃, M 87413-09-0 Martin's reagent
SOL 75-09-2 CH₂Cl₂
CON 30 minutes, room temperature

STAGE(2)
RGT N 7772-98-7 Na₂S₂O₃, L 144-55-8 NaHCO₃
SOL 7732-18-5 Water

PRO K 884313-58-0

RX(15) RCT AA 884313-62-6

STAGE(1)
RGT R 112246-73-8 Bicycloheptylborane, S 121-44-8 Et₃N
SOL 60-29-7 Et₂O
CON 1 hour, 0 deg C

STAGE(2)
RCT K 884313-58-0
SOL 60-29-7 Et₂O
CON SUBSTAGE(1) 3 hours, -78 deg C
SUBSTAGE(2) 16 hours, -20 deg C

STAGE(3)
RGT BJ 7722-84-1 H₂O₂
SOL 7732-18-5 Water, 67-56-1 MeOH
CON SUBSTAGE(1) 0 deg C, pH 7
SUBSTAGE(2) 1 hour, room temperature

PRO BI 884313-76-2
NTE stereoselective, buffered soln. in stage 3

RX(16)

STAGE(1)
RGT BK 109704-53-2 Me₄N.(AcO)₃BH, BL 64-19-7 AcOH
SOL 75-05-8 MeCN, 64-19-7 AcOH
CON 30 minutes, room temperature

STAGE(2)
RCT BI 884313-76-2
SOL 75-05-8 MeCN, 64-19-7 AcOH
CON SUBSTAGE(1) 0.5 hours, -30 deg C
SUBSTAGE(2) 1 hour, 0 deg C

STAGE(3)
RGT BG 304-59-6 Rochelle salt
SOL 7732-18-5 Water
CON 5 minutes

PRO W 884313--78--4

NTE stereoselective, in-situ generated reactant on stage 1

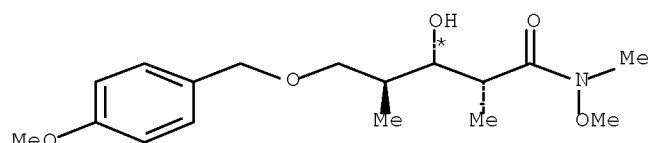
VERIFICATION INCOMPLETE - REACTION MAP DATA UNAVAILABLE

RX(106) OF 119 COMPOSED OF REACTION SEQUENCE RX(9), RX(5), RX(15), RX(16),
RX(4)

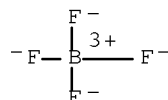
AND REACTION SEQUENCE RX(1), RX(10), RX(11), RX(12), RX(13),
RX(14), RX(2), RX(15), RX(16), RX(4)

...AP + AQ + Z ==> AA...

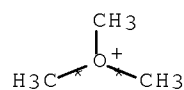
... A + B + AY + BD + AA ==> X



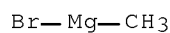
AP



AQ: CM 1

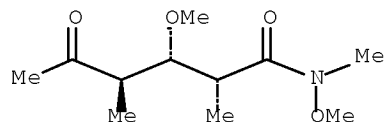


AQ: CM 2



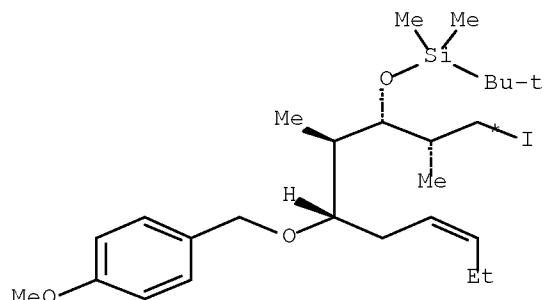
Z

10
STEPS
→

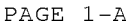


AA

START NEXT REACTION SEQUENCE



A





X
YIELD 92%

RX(9) RCT AP 252342-49-7, AQ 420-37-1
RGT AR 20734-58-1 Proton sponge
PRO Y 884313-70-6

RX(5) RCT Y 884313-70-6

STAGE(1)

RGT AB 1333-74-0 H₂
CAT 12135-22-7 Pd(OH)₂

STAGE(2)

RGT AC 67-68-5 DMSO, S 121-44-8 Et₃N, AD 79-37-8 (COCl)₂

STAGE(3)

RCT Z 75-16-1

PRO AA 884313-62-6

RX(1) RCT A 884313-56-8

STAGE(1)

RGT D 594-19-4 t-BuLi, E 7646-85-7 ZnCl₂
SOL 60-29-7 Et₂O, 109-66-0 Pentane
CON SUBSTAGE(1) 0.83 hours, -78 deg C
SUBSTAGE(2) 1 hour, room temperature

STAGE(2)

RCT B 212703-48-5
CAT 14221-01-3 Pd(PPh₃)₄
CON 15 hours, room temperature

STAGE(3)

RGT F 7732-18-5 Water

PRO C 884313-57-9

NTE in the dark in stage 2

RX(10) RCT C 884313-57-9

STAGE(1)

RGT AT 84-58-2 DDQ
SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
CON 30 minutes, 0 deg C

STAGE(2)

RGT AU 16940-66-2 NaBH4
SOL 67-56-1 MeOH
CON 10 minutes

PRO AS 884313-71-7

RX(11) RCT AS 884313-71-7

STAGE(1)

RGT AW 2564-83-2 Me4-piperidoxyl, AX 88-67-5 Benzoic acid,
2-iodo-
SOL 75-09-2 CH2Cl2
CON 2.5 hours, room temperature

STAGE(2)

RGT N 7772-98-7 Na2S2O3
SOL 7732-18-5 Water

PRO AV 884313-72-8

NTE chemoselective, regioselective

RX(12)

STAGE(1)

RGT BA 584-08-7 K2CO3, BB 17455-13-9 18-Crown-6
SOL 108-88-3 PhMe
CON 1 hour, room temperature

STAGE(2)

RCT AV 884313-72-8, AY 884313-77-3
SOL 108-88-3 PhMe
CON SUBSTAGE(1) 1 hour, -20 deg C
SUBSTAGE(2) 2 hours, 0 deg C

PRO AZ 884313-73-9

NTE stereoselective, Still-Gennari reaction

RX(13) RCT AZ 884313-73-9, BD 3019-71-4

STAGE(1)

SOL 75-09-2 CH2Cl2
CON 1 hour, room temperature

STAGE(2)

RGT BA 584-08-7 K2CO3
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 1.5 hours, room temperature

PRO BE 884313-74-0

RX(14) RCT BE 884313-74-0

STAGE(1)

RGT BF 1191-15-7 AlH(Bu-i)2
SOL 75-09-2 CH2Cl2, 110-54-3 Hexane
CON 25 minutes, -78 deg C

STAGE(2)

RGT BG 304-59-6 Rochelle salt

SOL 7732-18-5 Water
CON 1.5 hours, 0 deg C

PRO J 884313-75-1

RX(2) RCT J 884313-75-1

STAGE(1)
RGT L 144-55-8 NaHCO₃, M 87413-09-0 Martin's reagent
SOL 75-09-2 CH₂Cl₂
CON 30 minutes, room temperature

STAGE(2)
RGT N 7772-98-7 Na₂S₂O₃, L 144-55-8 NaHCO₃
SOL 7732-18-5 Water

PRO K 884313-58-0

RX(15) RCT AA 884313-62-6

STAGE(1)
RGT R 112246-73-8 Bicycloheptylborane, S 121-44-8 Et₃N
SOL 60-29-7 Et₂O
CON 1 hour, 0 deg C

STAGE(2)
RCT K 884313-58-0
SOL 60-29-7 Et₂O
CON SUBSTAGE(1) 3 hours, -78 deg C
SUBSTAGE(2) 16 hours, -20 deg C

STAGE(3)
RGT BJ 7722-84-1 H₂O₂
SOL 7732-18-5 Water, 67-56-1 MeOH
CON SUBSTAGE(1) 0 deg C, pH 7
SUBSTAGE(2) 1 hour, room temperature

PRO BI 884313-76-2
NTE stereoselective, buffered soln. in stage 3

RX(16)

STAGE(1)
RGT BK 109704-53-2 Me₄N.(AcO)₃BH, BL 64-19-7 AcOH
SOL 75-05-8 MeCN, 64-19-7 AcOH
CON 30 minutes, room temperature

STAGE(2)
RCT BI 884313-76-2
SOL 75-05-8 MeCN, 64-19-7 AcOH
CON SUBSTAGE(1) 0.5 hours, -30 deg C
SUBSTAGE(2) 1 hour, 0 deg C

STAGE(3)
RGT BG 304-59-6 Rochelle salt
SOL 7732-18-5 Water
CON 5 minutes

PRO W 884313-78-4
NTE stereoselective, in-situ generated reactant on stage 1

RX(4) RCT W 884313-78-4

STAGE(1)

RGT U 7647-01-0 HCl
SOL 7732-18-5 Water, 67-56-1 MeOH
CON 3 hours, room temperature

STAGE(2)

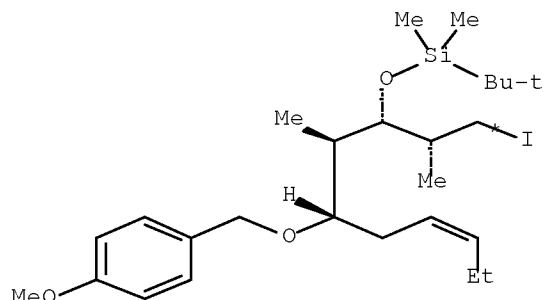
RGT L 144-55-8 NaHCO3
SOL 75-09-2 CH2Cl2
CON neutralized

PRO X 884313-60-4
NTE stereoselective

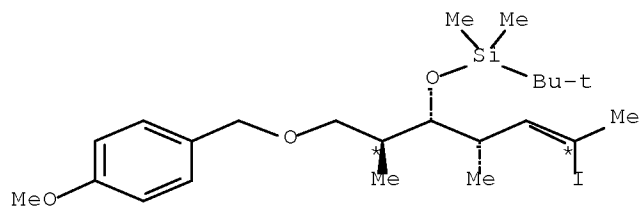
VERIFICATION INCOMPLETE - REACTION MAP DATA UNAVAILABLE

RX(111) OF 119 COMPOSED OF REACTION SEQUENCE RX(1), RX(10), RX(11), RX(12),
RX(13), RX(14), RX(2), RX(15)
AND REACTION SEQUENCE RX(9), RX(5), RX(15)

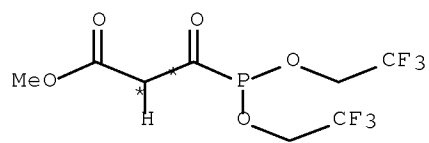
... A + B + AY + BD ==> K...
...AP + AQ + Z + K ==> BI



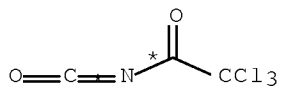
A



B

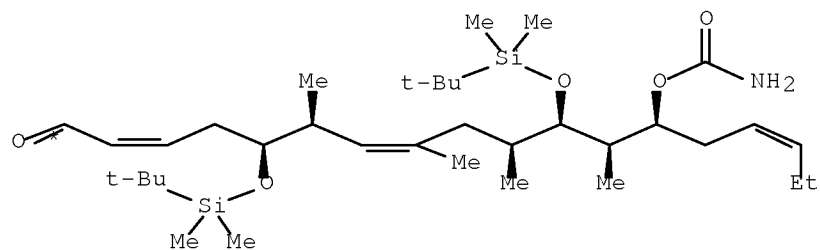


AY



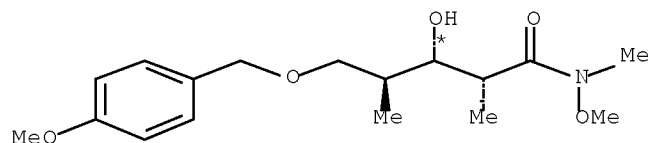
BD

3
STEPS
→

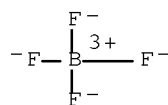


K

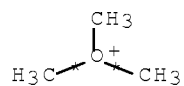
START NEXT REACTION SEQUENCE



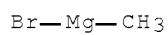
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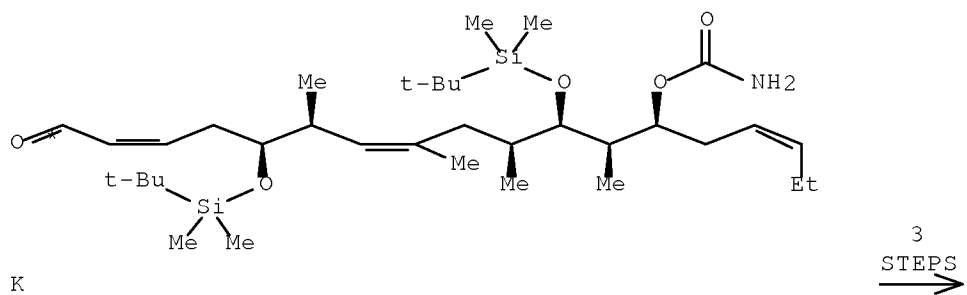
AQ: CM 1



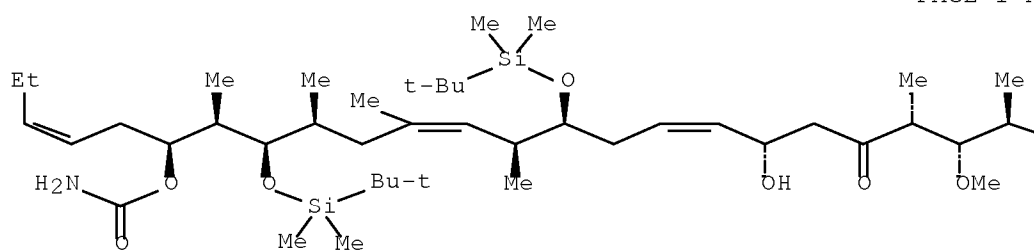
AQ: CM 2



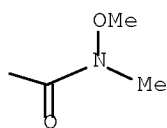
Z



PAGE 1-A



PAGE 1-B



BI
YIELD 87%

RX(1) RCT A 884313-56-8

STAGE(1)

RGT D 594-19-4 t-BuLi, E 7646-85-7 ZnCl2

SOL 60-29-7 Et2O, 109-66-0 Pentane

CON SUBSTAGE(1) 0.83 hours, -78 deg C

SUBSTAGE(2) 1 hour, room temperature

STAGE(2)

RCT B 212703-48-5

CAT 14221-01-3 Pd(PPh3)4

CON 15 hours, room temperature

STAGE(3)
 RGT F 7732-18-5 Water

 PRO C 884313-57-9
 NTE in the dark in stage 2

 RX(10) RCT C 884313-57-9

 STAGE(1)
 RGT AT 84-58-2 DDQ
 SOL 7732-18-5 Water, 75-09-2 CH2Cl2
 CON 30 minutes, 0 deg C

 STAGE(2)
 RGT AU 16940-66-2 NaBH4
 SOL 67-56-1 MeOH
 CON 10 minutes

 PRO AS 884313-71-7

 RX(11) RCT AS 884313-71-7

 STAGE(1)
 RGT AW 2564-83-2 Me4-piperidoxyl, AX 88-67-5 Benzoic acid,
 2-iodo-
 SOL 75-09-2 CH2Cl2
 CON 2.5 hours, room temperature

 STAGE(2)
 RGT N 7772-98-7 Na2S2O3
 SOL 7732-18-5 Water

 PRO AV 884313-72-8
 NTE chemoselective, regioselective

 RX(12)

 STAGE(1)
 RGT BA 584-08-7 K2CO3, BB 17455-13-9 18-Crown-6
 SOL 108-88-3 PhMe
 CON 1 hour, room temperature

 STAGE(2)
 RCT AV 884313-72-8, AY 884313-77-3
 SOL 108-88-3 PhMe
 CON SUBSTAGE(1) 1 hour, -20 deg C
 SUBSTAGE(2) 2 hours, 0 deg C

 PRO AZ 884313-73-9
 NTE stereoselective, Still-Gennari reaction

 RX(13) RCT AZ 884313-73-9, BD 3019-71-4

 STAGE(1)
 SOL 75-09-2 CH2Cl2
 CON 1 hour, room temperature

 STAGE(2)
 RGT BA 584-08-7 K2CO3
 SOL 67-56-1 MeOH

CON SUBSTAGE(1) 1 hour, 0 deg C
 SUBSTAGE(2) 1.5 hours, room temperature

PRO BE 884313-74-0

RX(14) RCT BE 884313-74-0

STAGE(1)
 RGT BF 1191-15-7 AlH(Bu-i)₂
 SOL 75-09-2 CH₂Cl₂, 110-54-3 Hexane
 CON 25 minutes, -78 deg C

STAGE(2)
 RGT BG 304-59-6 Rochelle salt
 SOL 7732-18-5 Water
 CON 1.5 hours, 0 deg C

PRO J 884313-75-1

RX(2) RCT J 884313-75-1

STAGE(1)
 RGT L 144-55-8 NaHCO₃, M 87413-09-0 Martin's reagent
 SOL 75-09-2 CH₂Cl₂
 CON 30 minutes, room temperature

STAGE(2)
 RGT N 7772-98-7 Na₂S₂O₃, L 144-55-8 NaHCO₃
 SOL 7732-18-5 Water

PRO K 884313-58-0

RX(9) RCT AP 252342-49-7, AQ 420-37-1
 RGT AR 20734-58-1 Proton sponge
 PRO Y 884313-70-6

RX(5) RCT Y 884313-70-6

STAGE(1)
 RGT AB 1333-74-0 H₂
 CAT 12135-22-7 Pd(OH)₂

STAGE(2)
 RGT AC 67-68-5 DMSO, S 121-44-8 Et₃N, AD 79-37-8 (COCl)₂

STAGE(3)
 RCT Z 75-16-1

PRO AA 884313-62-6

RX(15) RCT AA 884313-62-6

STAGE(1)
 RGT R 112246-73-8 Bicycloheptylborane, S 121-44-8 Et₃N
 SOL 60-29-7 Et₂O
 CON 1 hour, 0 deg C

STAGE(2)
 RCT K 884313-58-0
 SOL 60-29-7 Et₂O

CON SUBSTAGE(1) 3 hours, -78 deg C
 SUBSTAGE(2) 16 hours, -20 deg C

STAGE(3)

RGT BJ 7722-84-1 H2O2

SOL 7732-18-5 Water, 67-56-1 MeOH

CON SUBSTAGE(1) 0 deg C, pH 7

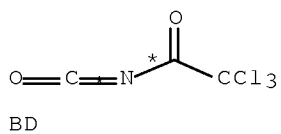
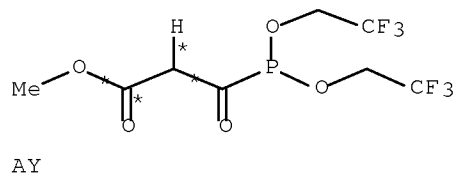
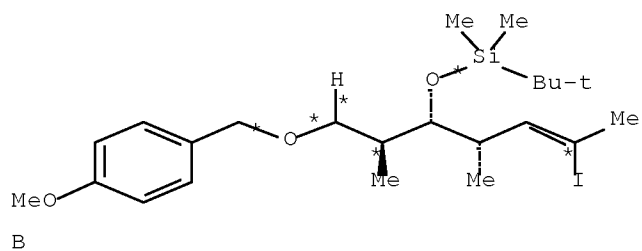
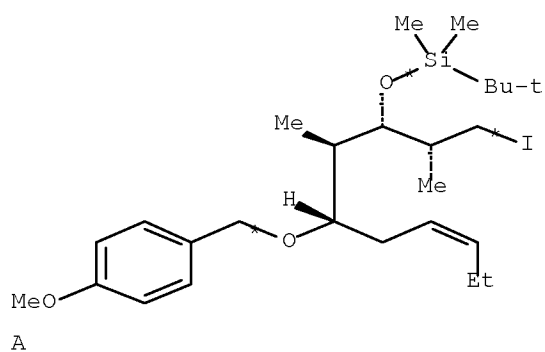
SUBSTAGE(2) 1 hour, room temperature

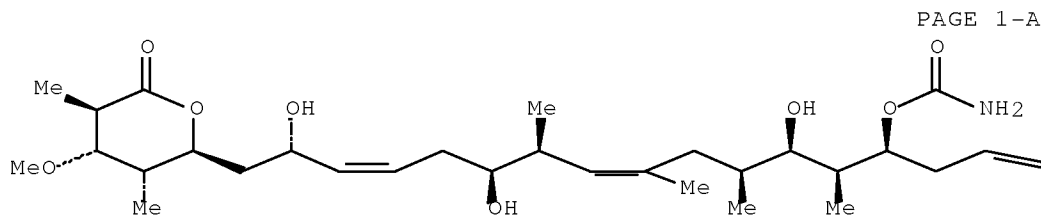
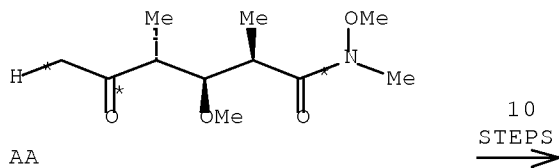
PRO BI 884313--76--2

NTE stereoselective, buffered soln. in stage 3

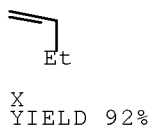
RX(115) OF 119 COMPOSED OF RX(1), RX(10), RX(11), RX(12), RX(13), RX(14),
 RX(2), RX(15), RX(16), RX(4)

RX(115) A + B + AY + BD + AA ==> X





PAGE 1-B



RX(1) RCT A 884313-56-8

STAGE(1)

RGT D 594-19-4 t-BuLi, E 7646-85-7 ZnCl₂
 SOL 60-29-7 Et₂O, 109-66-0 Pentane
 CON SUBSTAGE(1) 0.83 hours, -78 deg C
 SUBSTAGE(2) 1 hour, room temperature

STAGE(2)

RCT B 212703-48-5
 CAT 14221-01-3 Pd(PPh₃)₄
 CON 15 hours, room temperature

STAGE(3)

RGT F 7732-18-5 Water

PRO C 884313-57-9

NTE in the dark in stage 2

RX(10) RCT C 884313-57-9

STAGE(1)
RGT AT 84-58-2 DDQ
SOL 7732-18-5 Water, 75-09-2 CH2Cl2
CON 30 minutes, 0 deg C

STAGE(2)
RGT AU 16940-66-2 NaBH4
SOL 67-56-1 MeOH
CON 10 minutes

PRO AS 884313-71-7

RX(11) RCT AS 884313-71-7

STAGE(1)
RGT AW 2564-83-2 Me4-piperidoxyl, AX 88-67-5 Benzoic acid,
2-iodo-
SOL 75-09-2 CH2Cl2
CON 2.5 hours, room temperature

STAGE(2)
RGT N 7772-98-7 Na2S2O3
SOL 7732-18-5 Water

PRO AV 884313-72-8
NTE chemoselective, regioselective

RX(12)

STAGE(1)
RGT BA 584-08-7 K2CO3, BB 17455-13-9 18-Crown-6
SOL 108-88-3 PhMe
CON 1 hour, room temperature

STAGE(2)
RCT AV 884313-72-8, AY 884313-77-3
SOL 108-88-3 PhMe
CON SUBSTAGE(1) 1 hour, -20 deg C
SUBSTAGE(2) 2 hours, 0 deg C

PRO AZ 884313-73-9
NTE stereoselective, Still-Gennari reaction

RX(13) RCT AZ 884313-73-9, BD 3019-71-4

STAGE(1)
SOL 75-09-2 CH2Cl2
CON 1 hour, room temperature

STAGE(2)
RGT BA 584-08-7 K2CO3
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 1.5 hours, room temperature

PRO BE 884313-74-0

RX(14) RCT BE 884313-74-0

STAGE(1)
RGT BF 1191-15-7 AlH(Bu-i)2
SOL 75-09-2 CH2Cl2, 110-54-3 Hexane
CON 25 minutes, -78 deg C

STAGE(2)
RGT BG 304-59-6 Rochelle salt
SOL 7732-18-5 Water
CON 1.5 hours, 0 deg C

PRO J 884313-75-1

RX(2) RCT J 884313-75-1

STAGE(1)
RGT L 144-55-8 NaHCO3, M 87413-09-0 Martin's reagent
SOL 75-09-2 CH2Cl2
CON 30 minutes, room temperature

STAGE(2)
RGT N 7772-98-7 Na2S2O3, L 144-55-8 NaHCO3
SOL 7732-18-5 Water

PRO K 884313-58-0

RX(15) RCT AA 884313-62-6

STAGE(1)
RGT R 112246-73-8 Bicycloheptylborane, S 121-44-8 Et3N
SOL 60-29-7 Et2O
CON 1 hour, 0 deg C

STAGE(2)
RCT K 884313-58-0
SOL 60-29-7 Et2O
CON SUBSTAGE(1) 3 hours, -78 deg C
SUBSTAGE(2) 16 hours, -20 deg C

STAGE(3)
RGT BJ 7722-84-1 H2O2
SOL 7732-18-5 Water, 67-56-1 MeOH
CON SUBSTAGE(1) 0 deg C, pH 7
SUBSTAGE(2) 1 hour, room temperature

PRO BI 884313-76-2
NTE stereoselective, buffered soln. in stage 3

RX(16)

STAGE(1)
RGT BK 109704-53-2 Me4N.(AcO)3BH, BL 64-19-7 AcOH
SOL 75-05-8 MeCN, 64-19-7 AcOH
CON 30 minutes, room temperature

STAGE(2)
RCT BI 884313-76-2
SOL 75-05-8 MeCN, 64-19-7 AcOH
CON SUBSTAGE(1) 0.5 hours, -30 deg C
SUBSTAGE(2) 1 hour, 0 deg C

STAGE(3)

RGT BG 304-59-6 Rochelle salt
SOL 7732-18-5 Water
CON 5 minutes

PRO W 884313-78-4

NTE stereoselective, in-situ generated reactant on stage 1

RX(4) RCT W 884313-78-4

STAGE(1)

RGT U 7647-01-0 HCl
SOL 7732-18-5 Water, 67-56-1 MeOH
CON 3 hours, room temperature

STAGE(2)

RGT L 144-55-8 NaHCO3
SOL 75-09-2 CH2Cl2
CON neutralized

PRO X 884313-60-4

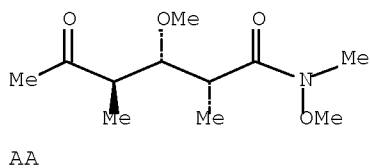
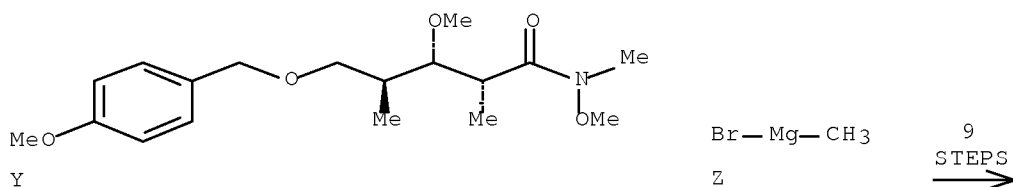
NTE stereoselective

VERIFICATION INCOMPLETE - REACTION MAP DATA UNAVAILABLE

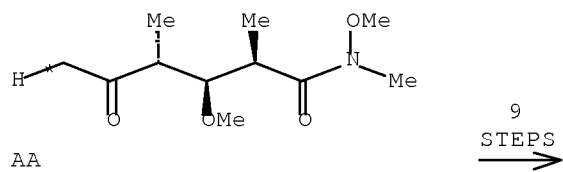
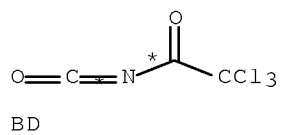
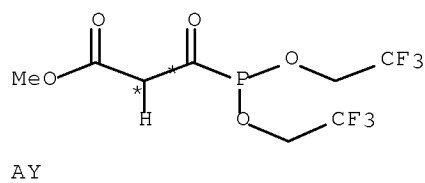
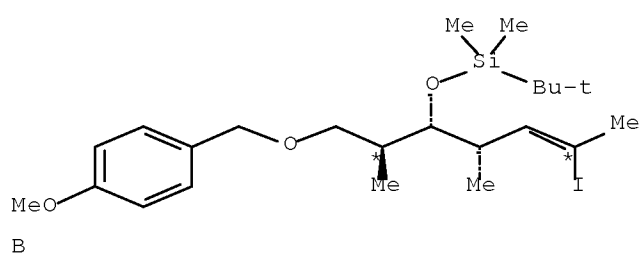
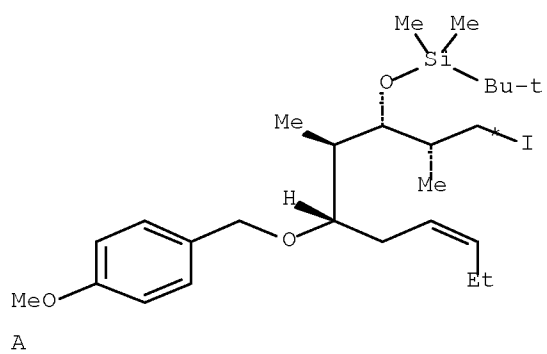
RX(117) OF 119 COMPOSED OF REACTION SEQUENCE RX(5), RX(15), RX(16)
AND REACTION SEQUENCE RX(1), RX(10), RX(11), RX(12), RX(13),
RX(14), RX(2), RX(15), RX(16)

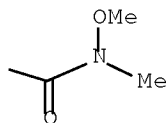
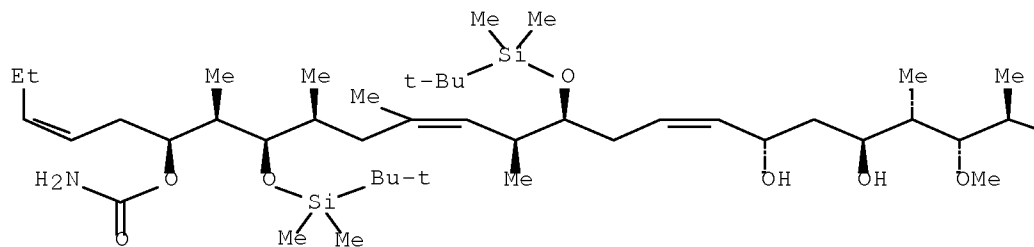
...Y + Z ==> AA...

... A + B + AY + BD + AA ==> W



START NEXT REACTION SEQUENCE





W
YIELD 81%

RX(5) RCT Y 884313-70-6

STAGE(1)

RGT AB 1333-74-0 H2

CAT 12135-22-7 Pd(OH)2

STAGE(2)

RGT AC 67-68-5 DMSO, S 121-44-8 Et3N, AD 79-37-8 (COCl)2

STAGE(3)

RCT Z 75-16-1

PRO AA 884313-62-6

RX(1) RCT A 884313-56-8

STAGE(1)

RGT D 594-19-4 t-BuLi, E 7646-85-7 ZnCl2

SOL 60-29-7 Et2O, 109-66-0 Pentane

CON SUBSTAGE(1) 0.83 hours, -78 deg C

SUBSTAGE(2) 1 hour, room temperature

STAGE(2)

RCT B 212703-48-5

CAT 14221-01-3 Pd(PPh3)4

CON 15 hours, room temperature

STAGE(3)

RGT F 7732-18-5 Water

PRO C 884313-57-9
NTE in the dark in stage 2

RX(10) RCT C 884313-57-9

STAGE(1)
RGT AT 84-58-2 DDQ
SOL 7732-18-5 Water, 75-09-2 CH2Cl2
CON 30 minutes, 0 deg C

STAGE(2)
RGT AU 16940-66-2 NaBH4
SOL 67-56-1 MeOH
CON 10 minutes

PRO AS 884313-71-7

RX(11) RCT AS 884313-71-7

STAGE(1)
RGT AW 2564-83-2 Me4-piperidoxyl, AX 88-67-5 Benzoic acid,
2-iodo-
SOL 75-09-2 CH2Cl2
CON 2.5 hours, room temperature

STAGE(2)
RGT N 7772-98-7 Na2S2O3
SOL 7732-18-5 Water

PRO AV 884313-72-8
NTE chemoselective, regioselective

RX(12)

STAGE(1)
RGT BA 584-08-7 K2CO3, BB 17455-13-9 18-Crown-6
SOL 108-88-3 PhMe
CON 1 hour, room temperature

STAGE(2)
RCT AV 884313-72-8, AY 884313-77-3
SOL 108-88-3 PhMe
CON SUBSTAGE(1) 1 hour, -20 deg C
SUBSTAGE(2) 2 hours, 0 deg C

PRO AZ 884313-73-9
NTE stereoselective, Still-Gennari reaction

RX(13) RCT AZ 884313-73-9, BD 3019-71-4

STAGE(1)
SOL 75-09-2 CH2Cl2
CON 1 hour, room temperature

STAGE(2)
RGT BA 584-08-7 K2CO3
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 1.5 hours, room temperature

PRO BE 884313-74-0

RX(14) RCT BE 884313-74-0

STAGE(1)

RGT BF 1191-15-7 AlH(Bu-i)₂
SOL 75-09-2 CH₂Cl₂, 110-54-3 Hexane
CON 25 minutes, -78 deg C

STAGE(2)

RGT BG 304-59-6 Rochelle salt
SOL 7732-18-5 Water
CON 1.5 hours, 0 deg C

PRO J 884313-75-1

RX(2) RCT J 884313-75-1

STAGE(1)

RGT L 144-55-8 NaHCO₃, M 87413-09-0 Martin's reagent
SOL 75-09-2 CH₂Cl₂
CON 30 minutes, room temperature

STAGE(2)

RGT N 7772-98-7 Na₂S₂O₃, L 144-55-8 NaHCO₃
SOL 7732-18-5 Water

PRO K 884313-58-0

RX(15) RCT AA 884313-62-6

STAGE(1)

RGT R 112246-73-8 Bicycloheptylborane, S 121-44-8 Et₃N
SOL 60-29-7 Et₂O
CON 1 hour, 0 deg C

STAGE(2)

RCT K 884313-58-0
SOL 60-29-7 Et₂O
CON SUBSTAGE(1) 3 hours, -78 deg C
SUBSTAGE(2) 16 hours, -20 deg C

STAGE(3)

RGT BJ 7722-84-1 H₂O₂
SOL 7732-18-5 Water, 67-56-1 MeOH
CON SUBSTAGE(1) 0 deg C, pH 7
SUBSTAGE(2) 1 hour, room temperature

PRO BI 884313-76-2

NTE stereoselective, buffered soln. in stage 3

RX(16)

STAGE(1)

RGT BK 109704-53-2 Me₄N.(AcO)₃BH, BL 64-19-7 AcOH
SOL 75-05-8 MeCN, 64-19-7 AcOH
CON 30 minutes, room temperature

STAGE(2)

RCT BI 884313-76-2

SOL 75-05-8 MeCN, 64-19-7 AcOH
 CON SUBSTAGE(1) 0.5 hours, -30 deg C
 SUBSTAGE(2) 1 hour, 0 deg C

STAGE(3)

RGT BG 304-59-6 Rochelle salt
 SOL 7732-18-5 Water
 CON 5 minutes

PRO W 884313--78--4

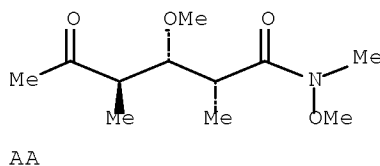
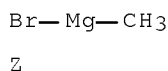
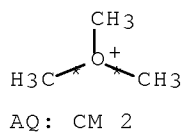
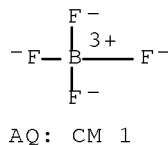
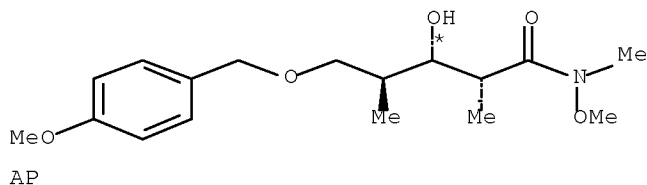
NTE stereoselective, in-situ generated reactant on stage 1

VERIFICATION INCOMPLETE - REACTION MAP DATA UNAVAILABLE

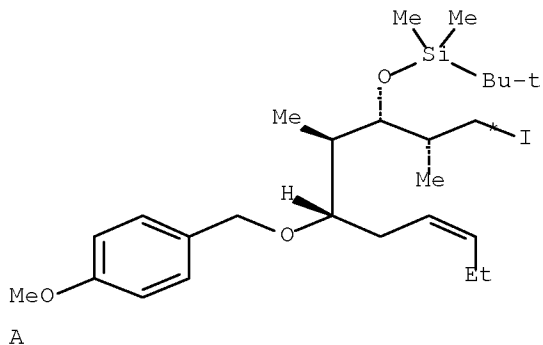
RX(118) OF 119 COMPOSED OF REACTION SEQUENCE RX(9), RX(5), RX(15), RX(16)
 AND REACTION SEQUENCE RX(1), RX(10), RX(11), RX(12), RX(13),
 RX(14), RX(2), RX(15), RX(16)

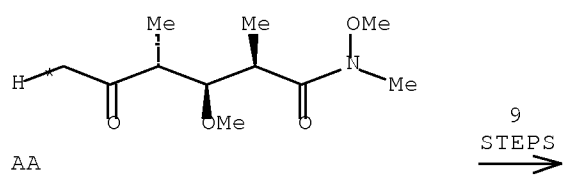
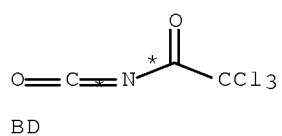
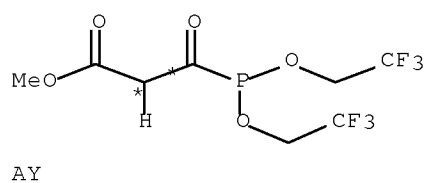
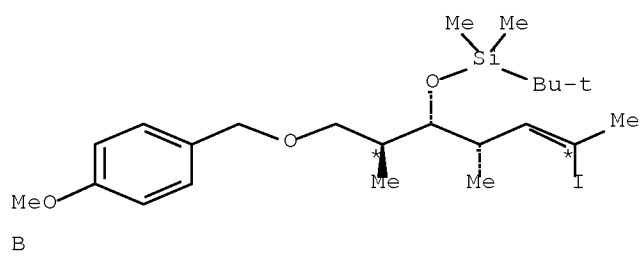
...AP + AQ + Z ==> AA...

... A + B + AY + BD + AA ==> W

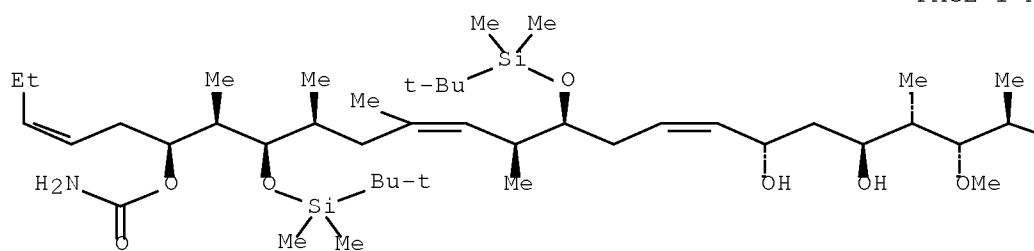


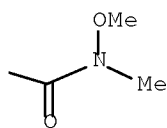
START NEXT REACTION SEQUENCE





PAGE 1-A





W
YIELD 81%

RX(9) RCT AP 252342-49-7, AQ 420-37-1
RGT AR 20734-58-1 Proton sponge
PRO Y 884313-70-6

RX(5) RCT Y 884313-70-6

STAGE(1)

RGT AB 1333-74-0 H2
CAT 12135-22-7 Pd(OH)2

STAGE(2)

RGT AC 67-68-5 DMSO, S 121-44-8 Et3N, AD 79-37-8 (COCl)2

STAGE(3)

RCT Z 75-16-1

PRO AA 884313-62-6

RX(1) RCT A 884313-56-8

STAGE(1)

RGT D 594-19-4 t-BuLi, E 7646-85-7 ZnCl2
SOL 60-29-7 Et2O, 109-66-0 Pentane
CON SUBSTAGE(1) 0.83 hours, -78 deg C
SUBSTAGE(2) 1 hour, room temperature

STAGE(2)

RCT B 212703-48-5
CAT 14221-01-3 Pd(PPh3)4
CON 15 hours, room temperature

STAGE(3)

RGT F 7732-18-5 Water

PRO C 884313-57-9

NTE in the dark in stage 2

RX(10) RCT C 884313-57-9

STAGE(1)

RGT AT 84-58-2 DDQ
SOL 7732-18-5 Water, 75-09-2 CH2Cl2
CON 30 minutes, 0 deg C

STAGE(2)

RGT AU 16940-66-2 NaBH4
SOL 67-56-1 MeOH
CON 10 minutes

PRO AS 884313-71-7

RX(11) RCT AS 884313-71-7

STAGE(1)

RGT AW 2564-83-2 Me4-piperidoxyl, AX 88-67-5 Benzoic acid,
2-iodo-
SOL 75-09-2 CH2Cl2
CON 2.5 hours, room temperature

STAGE(2)

RGT N 7772-98-7 Na2S2O3
SOL 7732-18-5 Water

PRO AV 884313-72-8

NTE chemoselective, regioselective

RX(12)

STAGE(1)

RGT BA 584-08-7 K2CO3, BB 17455-13-9 18-Crown-6
SOL 108-88-3 PhMe
CON 1 hour, room temperature

STAGE(2)

RCT AV 884313-72-8, AY 884313-77-3
SOL 108-88-3 PhMe
CON SUBSTAGE(1) 1 hour, -20 deg C
SUBSTAGE(2) 2 hours, 0 deg C

PRO AZ 884313-73-9

NTE stereoselective, Still-Gennari reaction

RX(13) RCT AZ 884313-73-9, BD 3019-71-4

STAGE(1)

SOL 75-09-2 CH2Cl2
CON 1 hour, room temperature

STAGE(2)

RGT BA 584-08-7 K2CO3
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 1.5 hours, room temperature

PRO BE 884313-74-0

RX(14) RCT BE 884313-74-0

STAGE(1)

RGT BF 1191-15-7 AlH(Bu-i)2
SOL 75-09-2 CH2Cl2, 110-54-3 Hexane
CON 25 minutes, -78 deg C

STAGE(2)

RGT BG 304-59-6 Rochelle salt

SOL 7732-18-5 Water
CON 1.5 hours, 0 deg C

PRO J 884313-75-1

RX(2) RCT J 884313-75-1

STAGE(1)

RGT L 144-55-8 NaHCO₃, M 87413-09-0 Martin's reagent
SOL 75-09-2 CH₂Cl₂
CON 30 minutes, room temperature

STAGE(2)

RGT N 7772-98-7 Na₂S₂O₃, L 144-55-8 NaHCO₃
SOL 7732-18-5 Water

PRO K 884313-58-0

RX(15) RCT AA 884313-62-6

STAGE(1)

RGT R 112246-73-8 Bicycloheptylborane, S 121-44-8 Et₃N
SOL 60-29-7 Et₂O
CON 1 hour, 0 deg C

STAGE(2)

RCT K 884313-58-0
SOL 60-29-7 Et₂O
CON SUBSTAGE(1) 3 hours, -78 deg C
SUBSTAGE(2) 16 hours, -20 deg C

STAGE(3)

RGT BJ 7722-84-1 H₂O₂
SOL 7732-18-5 Water, 67-56-1 MeOH
CON SUBSTAGE(1) 0 deg C, pH 7
SUBSTAGE(2) 1 hour, room temperature

PRO BI 884313-76-2

NTE stereoselective, buffered soln. in stage 3

RX(16)

STAGE(1)

RGT BK 109704-53-2 Me₄N.(AcO)₃BH, BL 64-19-7 AcOH
SOL 75-05-8 MeCN, 64-19-7 AcOH
CON 30 minutes, room temperature

STAGE(2)

RCT BI 884313-76-2
SOL 75-05-8 MeCN, 64-19-7 AcOH
CON SUBSTAGE(1) 0.5 hours, -30 deg C
SUBSTAGE(2) 1 hour, 0 deg C

STAGE(3)

RGT BG 304-59-6 Rochelle salt
SOL 7732-18-5 Water
CON 5 minutes

PRO W 884313-78-4

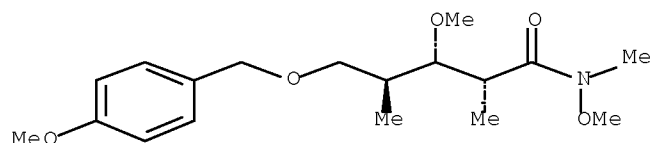
NTE stereoselective, in-situ generated reactant on stage 1

VERIFICATION INCOMPLETE - REACTION MAP DATA UNAVAILABLE

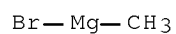
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AND REACTION SEQUENCE RX(1), RX(10), RX(11), RX(12), RX(13),
RX(14), RX(2), RX(15), RX(16), RX(4)

...Y + Z ==> AA...

... A + B + AY + BD + AA ==> X

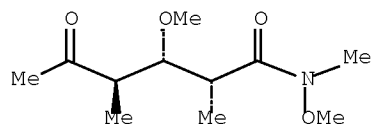


Y



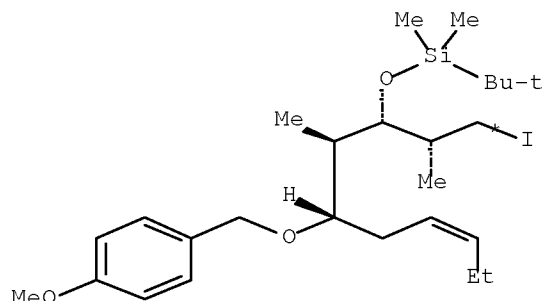
Z

10
STEPS
→

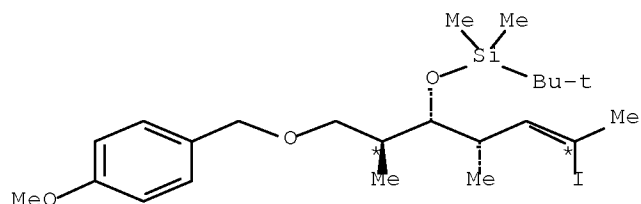


AA

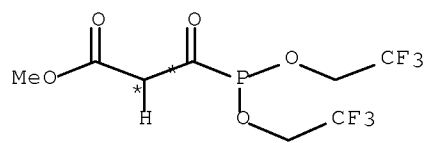
START NEXT REACTION SEQUENCE



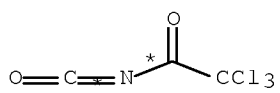
A



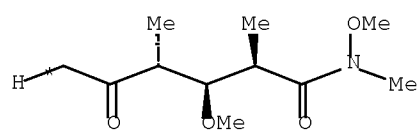
B



AY

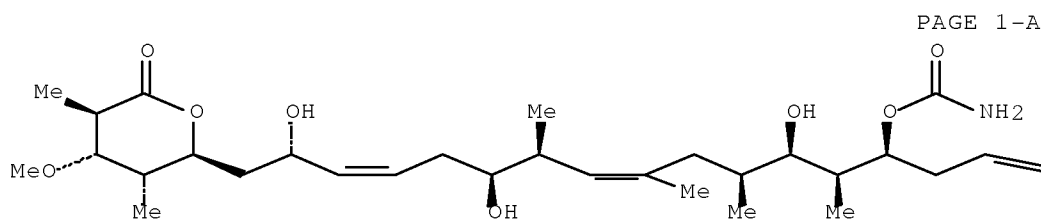


BD



AA

10
STEPS
➔



PAGE 1-A

PAGE 1-B



X
YIELD 92%

RX(5)

RCT Y 884313-70-6

STAGE(1)

RGT AB 1333-74-0 H2

CAT 12135-22-7 Pd(OH)₂

STAGE(2)

RGT AC 67-68-5 DMSO, S 121-44-8 Et₃N, AD 79-37-8 (COCl)₂

STAGE(3)

RCT Z 75-16-1

PRO AA 884313-62-6

RX(1) RCT A 884313-56-8

STAGE(1)

RGT D 594-19-4 t-BuLi, E 7646-85-7 ZnCl₂

SOL 60-29-7 Et₂O, 109-66-0 Pentane

CON SUBSTAGE(1) 0.83 hours, -78 deg C

SUBSTAGE(2) 1 hour, room temperature

STAGE(2)

RCT B 212703-48-5

CAT 14221-01-3 Pd(PPh₃)₄

CON 15 hours, room temperature

STAGE(3)

RGT F 7732-18-5 Water

PRO C 884313-57-9

NTE in the dark in stage 2

RX(10) RCT C 884313-57-9

STAGE(1)

RGT AT 84-58-2 DDQ

SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂

CON 30 minutes, 0 deg C

STAGE(2)

RGT AU 16940-66-2 NaBH₄

SOL 67-56-1 MeOH

CON 10 minutes

PRO AS 884313-71-7

RX(11) RCT AS 884313-71-7

STAGE(1)

RGT AW 2564-83-2 Me₄-piperidoxyl, AX 88-67-5 Benzoic acid,
2-iodo-

SOL 75-09-2 CH₂Cl₂

CON 2.5 hours, room temperature

STAGE(2)

RGT N 7772-98-7 Na₂S₂O₃

SOL 7732-18-5 Water

PRO AV 884313-72-8

NTE chemoselective, regioselective

RX(12)

STAGE(1)
 RGT BA 584-08-7 K2CO3, BB 17455-13-9 18-Crown-6
 SOL 108-88-3 PhMe
 CON 1 hour, room temperature

STAGE(2)
 RCT AV 884313-72-8, AY 884313-77-3
 SOL 108-88-3 PhMe
 CON SUBSTAGE(1) 1 hour, -20 deg C
 SUBSTAGE(2) 2 hours, 0 deg C

PRO AZ 884313-73-9
 NTE stereoselective, Still-Gennari reaction

RX(13) RCT AZ 884313-73-9, BD 3019-71-4

STAGE(1)
 SOL 75-09-2 CH2Cl2
 CON 1 hour, room temperature

STAGE(2)
 RGT BA 584-08-7 K2CO3
 SOL 67-56-1 MeOH
 CON SUBSTAGE(1) 1 hour, 0 deg C
 SUBSTAGE(2) 1.5 hours, room temperature

PRO BE 884313-74-0

RX(14) RCT BE 884313-74-0

STAGE(1)
 RGT BF 1191-15-7 AlH(Bu-i)2
 SOL 75-09-2 CH2Cl2, 110-54-3 Hexane
 CON 25 minutes, -78 deg C

STAGE(2)
 RGT BG 304-59-6 Rochelle salt
 SOL 7732-18-5 Water
 CON 1.5 hours, 0 deg C

PRO J 884313-75-1

RX(2) RCT J 884313-75-1

STAGE(1)
 RGT L 144-55-8 NaHCO3, M 87413-09-0 Martin's reagent
 SOL 75-09-2 CH2Cl2
 CON 30 minutes, room temperature

STAGE(2)
 RGT N 7772-98-7 Na2S2O3, L 144-55-8 NaHCO3
 SOL 7732-18-5 Water

PRO K 884313-58-0

RX(15) RCT AA 884313-62-6

STAGE(1)
 RGT R 112246-73-8 Bicycloheptylborane, S 121-44-8 Et3N
 SOL 60-29-7 Et2O

CON 1 hour, 0 deg C

STAGE(2)

RCT K 884313-58-0

SOL 60-29-7 Et2O

CON SUBSTAGE(1) 3 hours, -78 deg C

SUBSTAGE(2) 16 hours, -20 deg C

STAGE(3)

RGT BJ 7722-84-1 H2O2

SOL 7732-18-5 Water, 67-56-1 MeOH

CON SUBSTAGE(1) 0 deg C, pH 7

SUBSTAGE(2) 1 hour, room temperature

PRO BI 884313-76-2

NTE stereoselective, buffered soln. in stage 3

RX(16)

STAGE(1)

RGT BK 109704-53-2 Me4N.(AcO)3BH, BL 64-19-7 AcOH

SOL 75-05-8 MeCN, 64-19-7 AcOH

CON 30 minutes, room temperature

STAGE(2)

RCT BI 884313-76-2

SOL 75-05-8 MeCN, 64-19-7 AcOH

CON SUBSTAGE(1) 0.5 hours, -30 deg C

SUBSTAGE(2) 1 hour, 0 deg C

STAGE(3)

RGT BG 304-59-6 Rochelle salt

SOL 7732-18-5 Water

CON 5 minutes

PRO W 884313-78-4

NTE stereoselective, in-situ generated reactant on stage 1

RX(4)

RCT W 884313-78-4

STAGE(1)

RGT U 7647-01-0 HCl

SOL 7732-18-5 Water, 67-56-1 MeOH

CON 3 hours, room temperature

STAGE(2)

RGT L 144-55-8 NaHCO3

SOL 75-09-2 CH2Cl2

CON neutralized

PRO X 884313-60-4

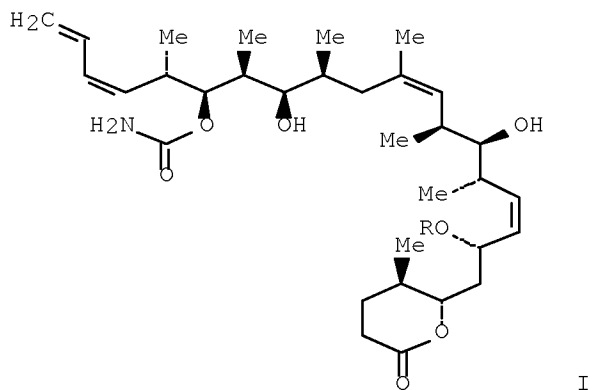
NTE stereoselective

L3 ANSWER 4 OF 9 CASREACT COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 144:6608 CASREACT Full-text

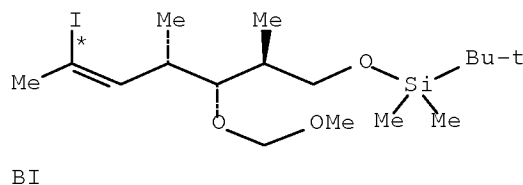
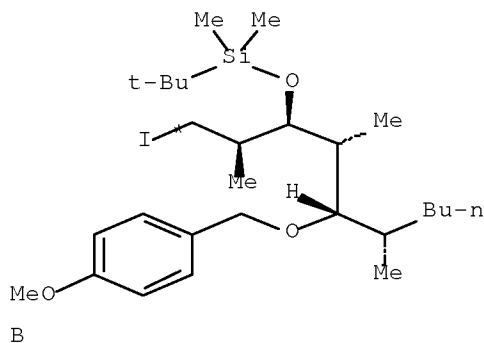
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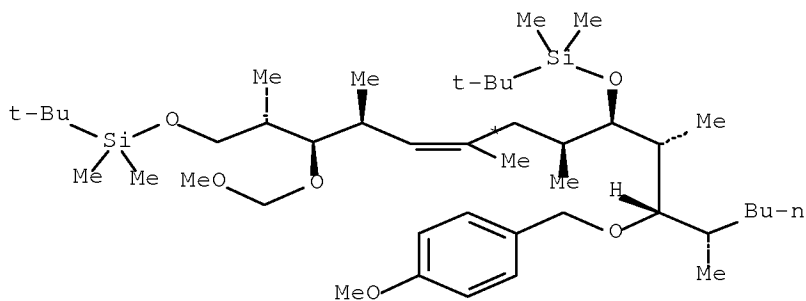
AUTHOR(S): Smith, Amos B., III; Xian, Ming
 CORPORATE SOURCE: Department of Chemistry, Monell Chemical Senses Center, and Laboratory for Research on the Structure of Matter, University of Pennsylvania, Philadelphia, PA, 19104, USA
 SOURCE: Organic Letters (2005), 7(23), 5229-5232
 CODEN: ORLEF7; ISSN: 1523-7060
 PUBLISHER: American Chemical Society
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI



AB The design, synthesis, and biol. evaluation of seven totally synthetic analogs of the antitumor agent (+)-discodermolide are reported. For example, discodermolide analog I (R = H) reacted with methoxymethyl chloride to give I (R = CH₂OMe) in 40% yield. Saturation of the terminal diene system, alteration of the substituents on the lactone, and alkylation of the C(7)-hydroxyl group reveal significant structure-activity relationships.
 REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(20) OF 268 ...E + BI ==> EJ...





BJ
YIELD 82%

```

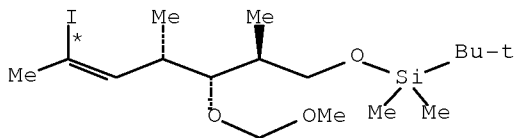
RX(20)      RCT  B 870074-98-9, BI 852049-56-0
            RGT  BK 534-17-8 Cs2CO3
            PRO  BJ 870075-18-6
            CAT  72287-26-4 Palladium, [1,1'-bis(diphenylphosphino-
            κP)ferrocene]dichloro-, (SP-4-2)-
            NTE  Suzuki coupling

```

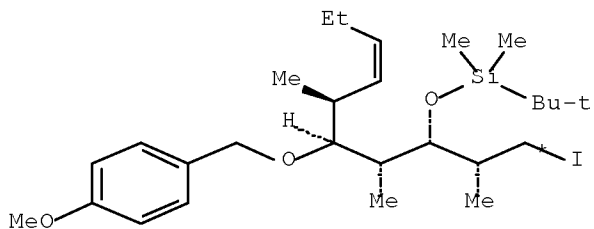
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RX(27) OF 268      ...BI  +  Y  ==>  BV...

```

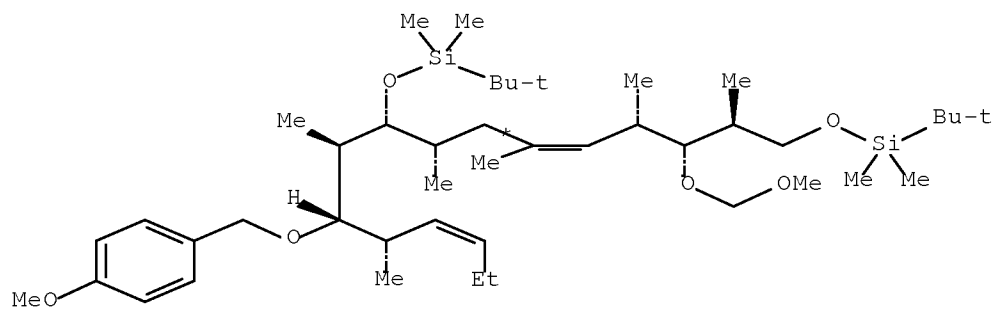


BI



Y

(27)

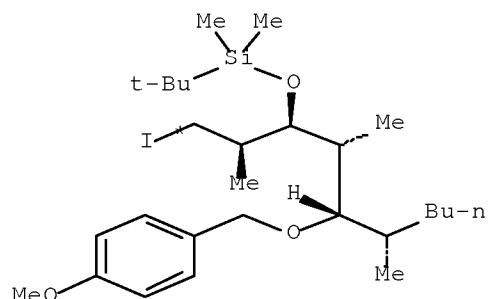


BV
YIELD 85%

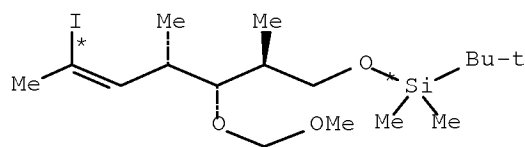
RX(27) RCT BI 852049-56-0, Y 870075-02-8
 RGT BK 534-17-8 Cs₂CO₃
 PRO BV 870075-26-6
 CAT 72287-26-4 Palladium, [1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-, (SP-4-2)-
 NTE Suzuki coupling

RX(55) OF 268 COMPOSED OF RX(20), RX(21)

RX(55) E + BI ==> I

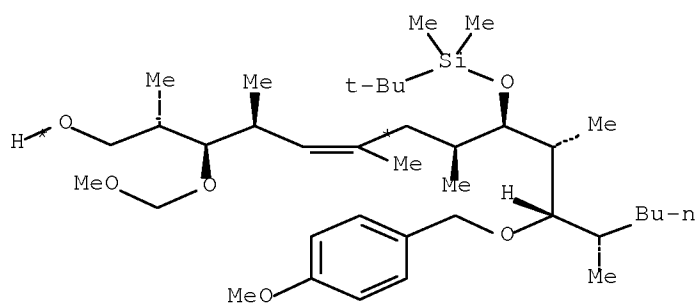


B



BI

2
STEPS
→



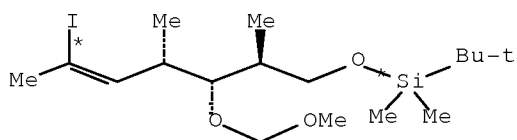
I
YIELD 90%

RX(20) RCT B 870074-98-9, BI 852049-56-0
 RGT BK 534-17-8 Cs₂CO₃
 PRO BJ 870075-18-6
 CAT 72287-26-4 Palladium, [1,1'-bis(diphenylphosphino)-
 κP]ferrocene]dichloro-, (SP-4-2)-
 NTE Suzuki coupling

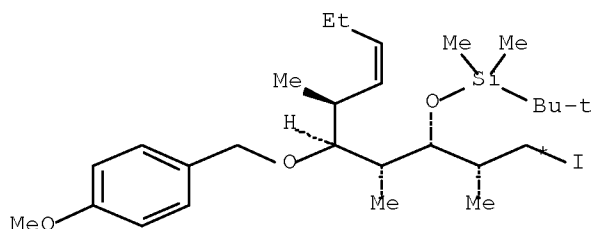
RX(21) RCT BJ 870075-18-6
 RGT W 7647-01-0 HCl
 PRO I 870075-19-7
 SOL 7732-18-5 Water

RX(62) OF 268 COMPOSED OF RX(27), RX(28)

RX(62) BI + Y ==> BW

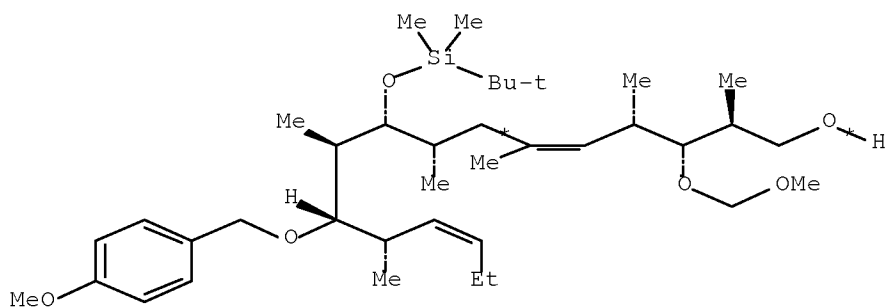


BI



Y

2
STEPS
→

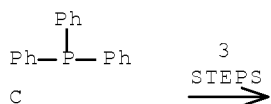
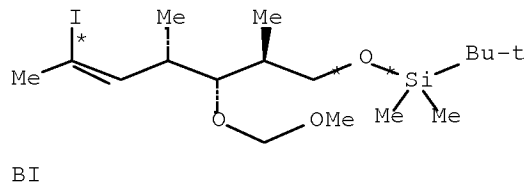
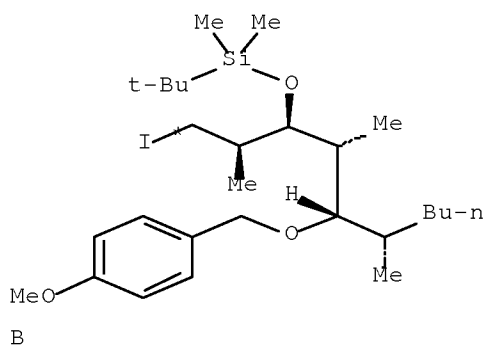


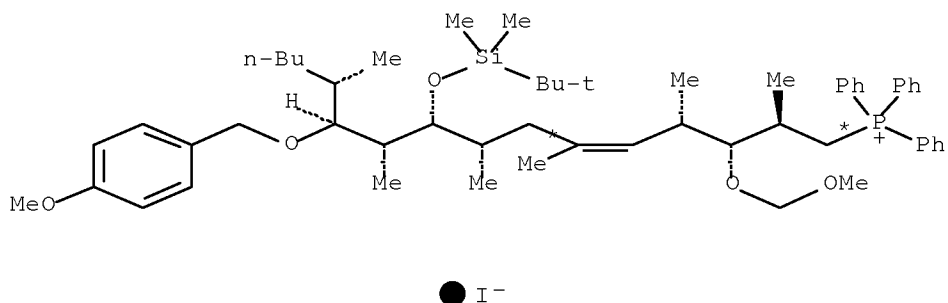
BW
YIELD 90%

RX(27) RCT BI 852049-56-0, Y 870075-02-8
 RGT BK 534-17-8 Cs2CO3
 PRO BV 870075-26-6
 CAT 72287-26-4 Palladium, [1,1'-bis(diphenylphosphino-
 κP)ferrocene]dichloro-, (SP-4-2)-
 NTE Suzuki coupling

RX(28) RCT BV 870075-26-6
 RGT W 7647-01-0 HCl
 PRO BW 870075-27-7
 SOL 7732-18-5 Water
 NTE regioselective

RX(104) OF 268 COMPOSED OF RX(20), RX(21), RX(2)
 RX(104) B + BI + C ==> J





J
YIELD 89%

```

RX(20)    RCT  B 870074-98-9, BI 852049-56-0
          RGT  BK 534-17-8 Cs2CO3
          PRO  BJ 870075-18-6
          CAT  72287-26-4 Palladium, [1,1'-bis(diphenylphosphino-
          κP)ferrocene]dichloro-, (SP-4-2)-
          NTE  Suzuki coupling

RX(21)    RCT  BJ 870075-18-6
          RGT  W 7647-01-0 HCl
          PRO  I 870075-19-7
          SOL  7732-18-5 Water

RX(2)     RCT  I 870075-19-7

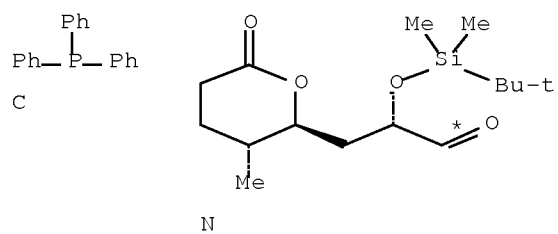
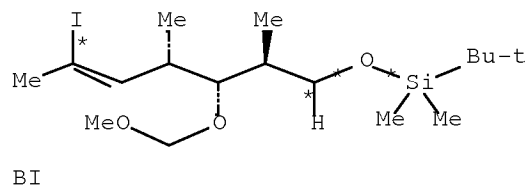
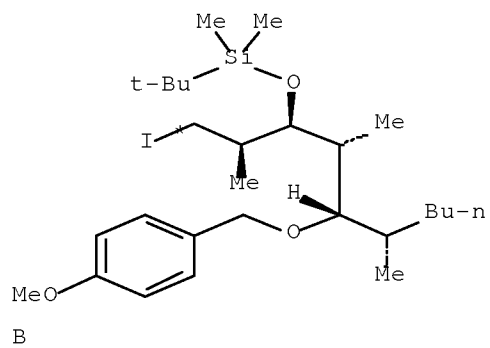
          STAGE(1)
          RGT  K 7553-56-2 I2, C 603-35-0 PPh3, D 288-32-4 1H-Imidazole

          STAGE(2)
          RCT  C 603-35-0
          RGT  L 121-44-8 Et3N
          CON  100 deg C

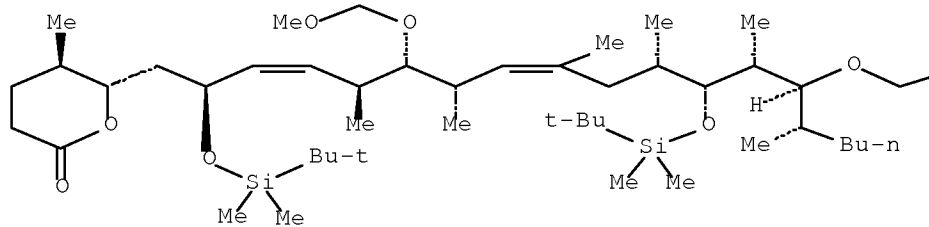
          PRO  J 870074-99-0
          NTE  Wittig salt formation in second stage, yield over 4 steps = 65%

RX(107)   OF 268 COMPOSED OF RX(20), RX(21), RX(2), RX(23)
RX(107)   E  +  BI  +  C  +  N  ==>  R

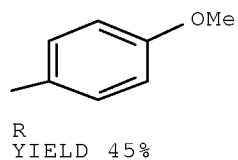
```



4
STEPS
→



PAGE 1-A



PAGE 1-B

RX(20) RCT B 870074-98-9, BI 852049-56-0
 RGT BK 534-17-8 Cs2CO3

PRO BJ 870075-18-6
 CAT 72287-26-4 Palladium, [1,1'-bis(diphenylphosphino-
 κP)ferrocene]dichloro-, (SP-4-2)-
 NTE Suzuki coupling

RX(21) RCT BJ 870075-18-6
 RGT W 7647-01-0 HCl
 PRO I 870075-19-7
 SOL 7732-18-5 Water

RX(2) RCT I 870075-19-7

STAGE(1)

RGT K 7553-56-2 I2, C 603-35-0 PPh3, D 288-32-4 1H-Imidazole

STAGE(2)

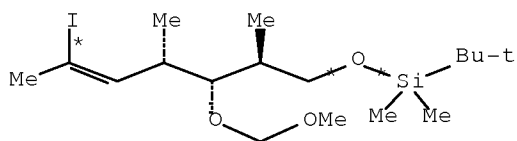
RCT C 603-35-0
 RGT L 121-44-8 Et3N
 CON 100 deg C

PRO J 870074-99-0

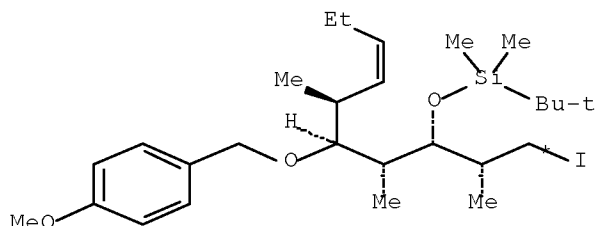
NTE Wittig salt formation in second stage, yield over 4 steps = 65%

RX(23) RCT J 870074-99-0, N 853055-22-8
 RGT AI 917-54-4 MeLi
 PRO R 870075-21-1
 NTE stereoselective, Wittig coupling

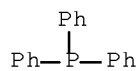
RX(116) OF 268 COMPOSED OF RX(27), RX(28), RX(29)
 RX(116) BI + Y + C ==> BX



BI

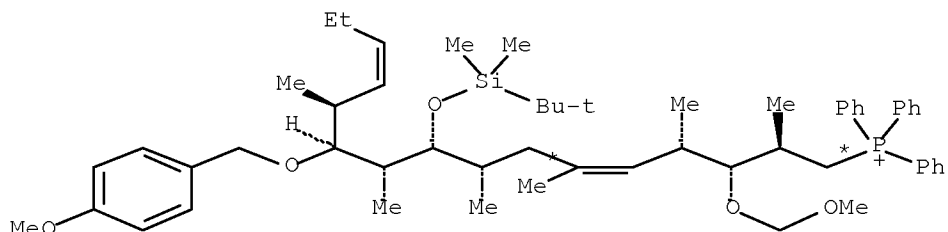


Y



C

3
 STEPS
 →



BX
YIELD 85%

RX(27) RCT BI 852049-56-0, Y 870075-02-8
RGT BK 534-17-8 Cs2CO3
PRO BV 870075-26-6
CAT 72287-26-4 Palladium, [1,1'-bis(diphenylphosphino-
κP)ferrocene]dichloro-, (SP-4-2)-
NTE Suzuki coupling

RX(28) RCT BV 870075-26-6
RGT W 7647-01-0 HCl
PRO BW 870075-27-7
SOL 7732-18-5 Water
NTE regioselective

RX(29) RCT BW 870075-27-7

STAGE(1)

RGT K 7553-56-2 I2, C 603-35-0 PPh3, D 288-32-4 1H-Imidazole

STAGE(2)

RCT C 603-35-0

RGT L 121-44-8 Et3N

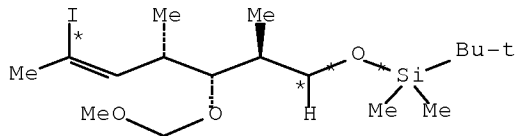
CON 100 deg C

PRO BX 870075-28-8

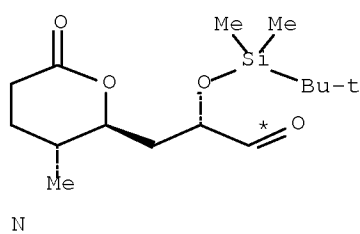
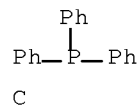
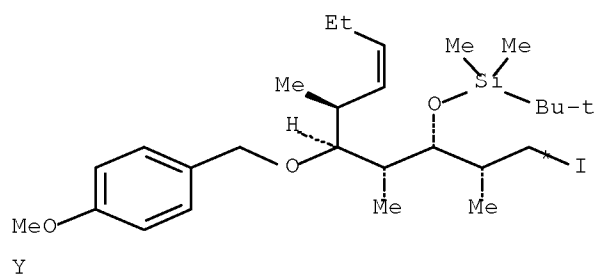
NTE stereoselective, Wittig salt formation in second stage

RX(119) OF 268 COMPOSED OF RX(27), RX(28), RX(29), RX(30)

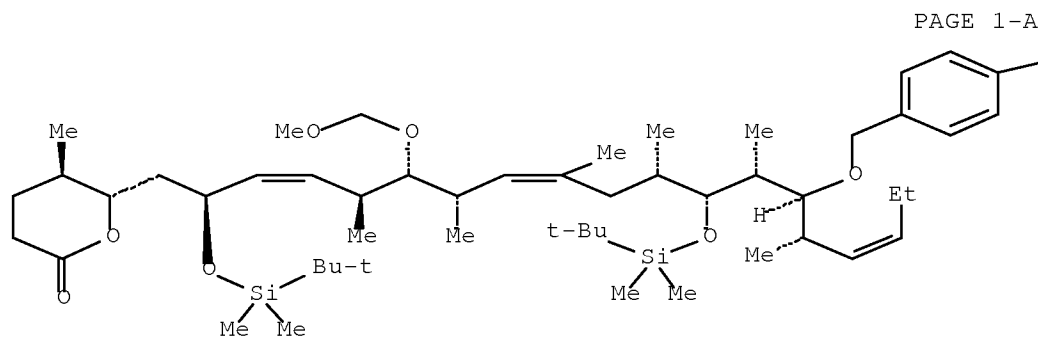
RX(119) BI + Y + C + N ==> EY



BI



4
STEPS
→



—OMe
BY
YIELD 50%

PAGE 1-B

RX(27) RCT BI 852049-56-0, Y 870075-02-8
RGT BK 534-17-8 Cs2CO3

PRO BV 870075-26-6
 CAT 72287-26-4 Palladium, [1,1'-bis(diphenylphosphino-
 κP)ferrocene]dichloro-, (SP-4-2)-
 NTE Suzuki coupling

RX(28) RCT BV 870075-26-6
 RGT W 7647-01-0 HCl
 PRO BW 870075-27-7
 SOL 7732-18-5 Water
 NTE regioselective

RX(29) RCT BW 870075-27-7

STAGE(1)

RGT K 7553-56-2 I2, C 603-35-0 PPh3, D 288-32-4 1H-Imidazole

STAGE(2)

RCT C 603-35-0
 RGT L 121-44-8 Et3N
 CON 100 deg C

PRO BX 870075-28-8
 NTE stereoselective, Wittig salt formation in second stage

RX(30) RCT N 853055-22-8, BX 870075-28-8
 RGT AU 1333-74-0 H2
 PRO BY 870075-29-9
 CAT 12135-22-7 Pd(OH)2
 SOL 141-78-6 AcOEt
 NTE Wittig coupling

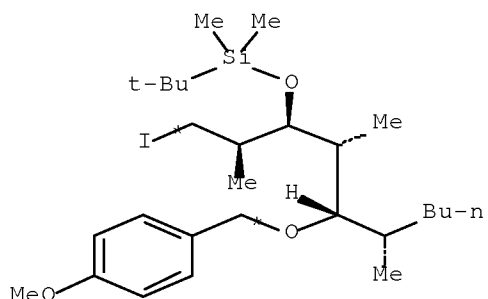
RX(151) OF 268 COMPOSED OF REACTION SEQUENCE RX(3), RX(23), RX(4)
 AND REACTION SEQUENCE RX(20), RX(21), RX(2), RX(23), RX(4)

...M ==> N...

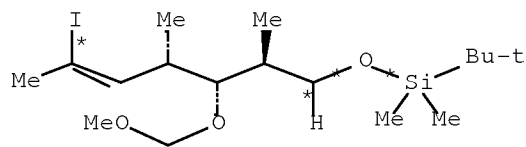
... B + BI + C + N ==> S



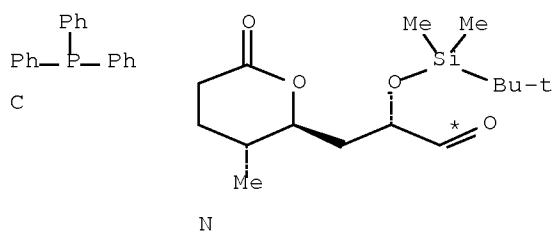
START NEXT REACTION SEQUENCE



B



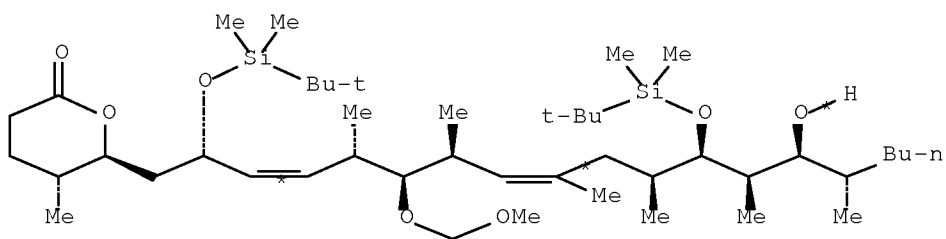
BI



C

N

5
STEPS
→



S
YIELD 80%

RX(3) RCT M 870075-20-0

STAGE(1)

RGT E 144-55-8 NaHCO₃, O 87413-09-0 Martin's reagent
SOL 75-09-2 CH₂Cl₂
CON 2.5 hours, room temperature

STAGE(2)

RGT P 7772-98-7 Na₂S₂O₃, E 144-55-8 NaHCO₃
SOL 7732-18-5 Water
CON room temperature

PRO N 853055-22-8

RX(20) RCT B 870074-98-9, BI 852049-56-0
RGT BK 534-17-8 Cs2CO3
PRO BJ 870075-18-6
CAT 72287-26-4 Palladium, [1,1'-bis(diphenylphosphino-
κP)ferrocene]dichloro-, (SP-4-2)-
NTE Suzuki coupling

RX(21) RCT BJ 870075-18-6
RGT W 7647-01-0 HCl
PRO I 870075-19-7
SOL 7732-18-5 Water

RX(2) RCT I 870075-19-7

STAGE(1)

RGT K 7553-56-2 I2, C 603-35-0 PPh3, D 288-32-4 1H-Imidazole

STAGE(2)

RCT C 603-35-0
RGT L 121-44-8 Et3N
CON 100 deg C

PRO J 870074-99-0

NTE Wittig salt formation in second stage, yield over 4 steps = 65%

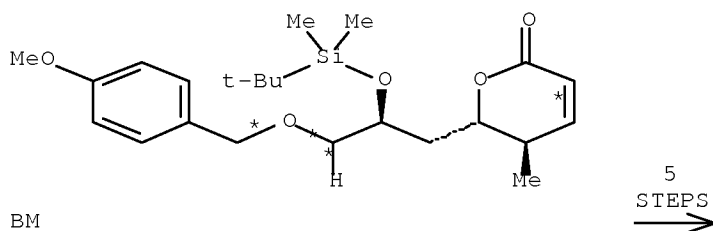
RX(23) RCT J 870074-99-0, N 853055-22-8
RGT AI 917-54-4 MeLi
PRO R 870075-21-1
NTE stereoselective, Wittig coupling

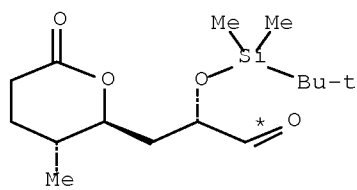
RX(4) RCT R 870075-21-1
RGT T 84-58-2 DDQ
PRO S 870075-00-6
NTE yield over 2 steps = 36%

RX(152) OF 268 COMPOSED OF REACTION SEQUENCE RX(22), RX(3), RX(23), RX(4)
AND REACTION SEQUENCE RX(20), RX(21), RX(2), RX(23), RX(4)

...BM ==> N...

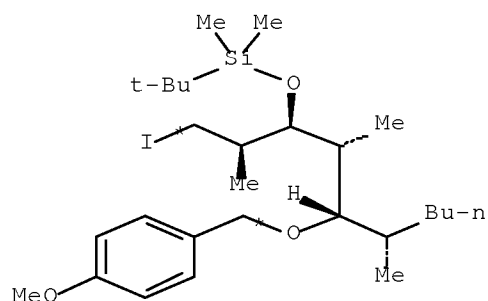
... B + BI + C + N ==> S



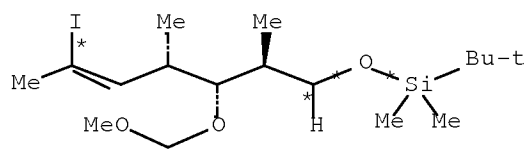


N

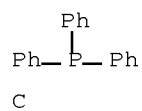
START NEXT REACTION SEQUENCE



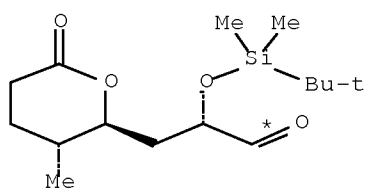
B



BI

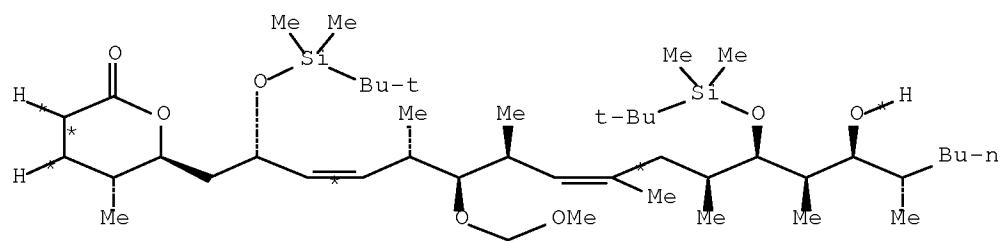


C



N

5
STEPS
→



S
YIELD 80%

RX(22) RCT BM 837383-29-6
 RGT AU 1333-74-0 H2
 PRO M 870075-20-0
 CAT 12135-22-7 Pd(OH)2
 SOL 141-78-6 AcOEt

RX(3) RCT M 870075-20-0

STAGE(1)
 RGT E 144-55-8 NaHCO3, O 87413-09-0 Martin's reagent
 SOL 75-09-2 CH2Cl2
 CON 2.5 hours, room temperature

STAGE(2)
 RGT P 7772-98-7 Na2S2O3, E 144-55-8 NaHCO3
 SOL 7732-18-5 Water
 CON room temperature

PRO N 853055-22-8

RX(20) RCT B 870074-98-9, BI 852049-56-0
 RGT BK 534-17-8 Cs2CO3
 PRO BJ 870075-18-6
 CAT 72287-26-4 Palladium, [1,1'-bis(diphenylphosphino-
 κP)ferrocene]dichloro-, (SP-4-2)-
 NTE Suzuki coupling

RX(21) RCT BJ 870075-18-6
 RGT W 7647-01-0 HCl
 PRO I 870075-19-7
 SOL 7732-18-5 Water

RX(2) RCT I 870075-19-7

STAGE(1)
 RGT K 7553-56-2 I2, C 603-35-0 PPh3, D 288-32-4 1H-Imidazole

STAGE(2)
 RCT C 603-35-0
 RGT L 121-44-8 Et3N
 CON 100 deg C

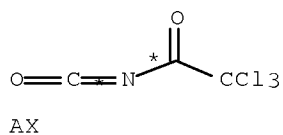
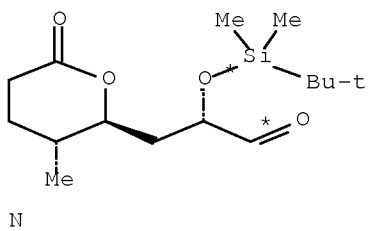
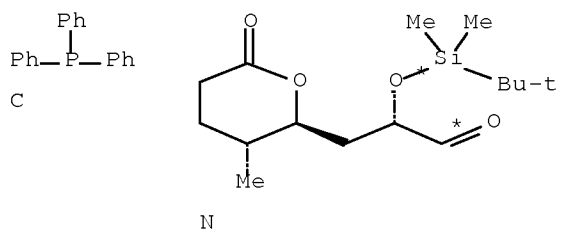
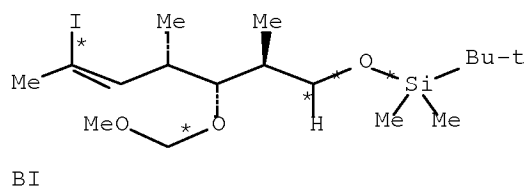
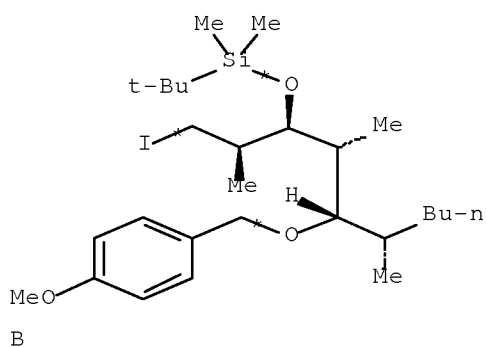
PRO J 870074-99-0
 NTE Wittig salt formation in second stage, yield over 4 steps = 65%

RX(23) RCT J 870074-99-0, N 853055-22-8
 RGT AI 917-54-4 MeLi
 PRO R 870075-21-1
 NTE stereoselective, Wittig coupling

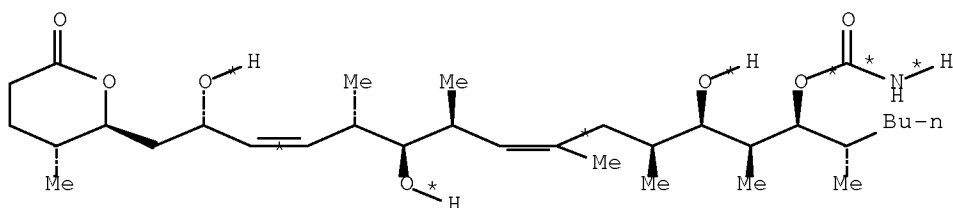
RX(4) RCT R 870075-21-1
 RGT T 84-58-2 DDQ
 PRO S 870075-00-6
 NTE yield over 2 steps = 36%

RX(153) OF 268 COMPOSED OF RX(20), RX(21), RX(2), RX(23), RX(4), RX(24), RX(5)

RX(153) B + BI + C + N + AX ==> V



7
STEPS
→



YIELD 63%

RX(20) RCT B 870074-98-9, BI 852049-56-0
 RGT BK 534-17-8 Cs₂CO₃
 PRO BJ 870075-18-6
 CAT 72287-26-4 Palladium, [1,1'-bis(diphenylphosphino-
 κP)ferrocene]dichloro-, (SP-4-2)-
 NTE Suzuki coupling

RX(21) RCT BJ 870075-18-6
 RGT W 7647-01-0 HCl
 PRO I 870075-19-7
 SOL 7732-18-5 Water

RX(2) RCT I 870075-19-7

STAGE(1)
RGT K 7553-56-2 I2, C 603-35-0 PPh3, D 288-32-4 1H-Imidazole

STAGE(2)
RCT C 603-35-0
RGT L 121-44-8 Et3N
CON 100 deg C

PRO J 870074-99-0
NTE Wittig salt formation in second stage, yield over 4 steps = 65%

RX(23) RCT J 870074-99-0, N 853055-22-8
RGT AI 917-54-4 MeLi
PRO R 870075-21-1
NTE stereoselective, Wittig coupling

RX(4) RCT R 870075-21-1
RGT T 84-58-2 DDQ
PRO S 870075-00-6
NTE yield over 2 steps = 36%

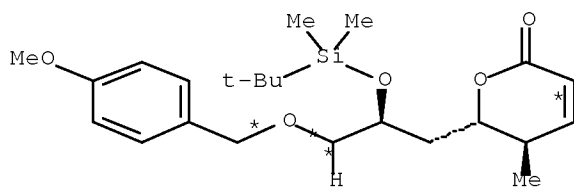
RX(24) RCT S 870075-00-6, AX 3019-71-4
PRO U 870075-22-2
NTE literature preparation

RX(5) RCT U 870075-22-2
RGT W 7647-01-0 HCl
PRO V ~~870075-01-7~~
SOL 7732-18-5 Water
NTE yield over 2 steps = 54%

RX(154) OF 268 COMPOSED OF REACTION SEQUENCE RX(22), RX(3), RX(23)
AND REACTION SEQUENCE RX(20), RX(21), RX(2), RX(23)

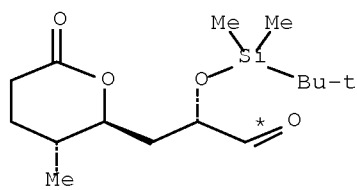
...BM ==> N...

... B + BI + C + N ==> R



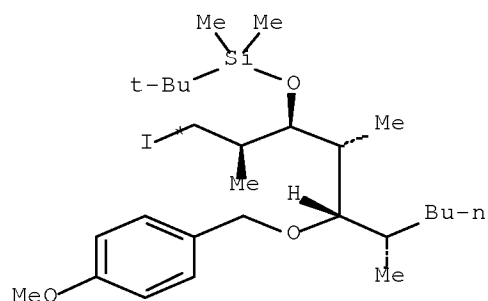
BM

4
STEPS
→

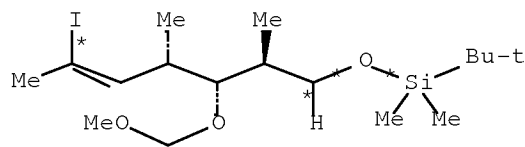


N

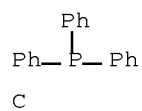
START NEXT REACTION SEQUENCE



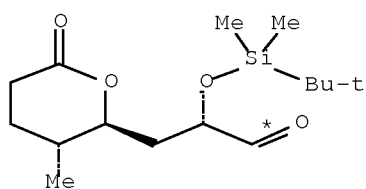
B



BI



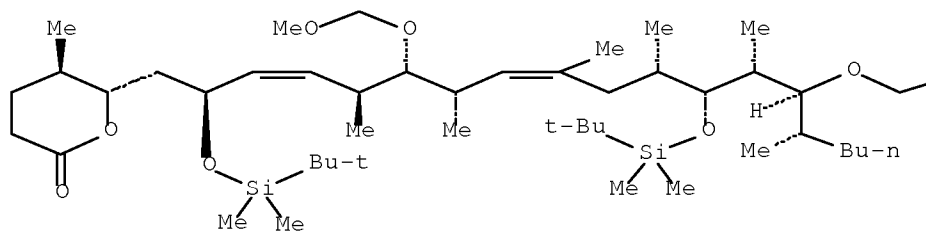
C

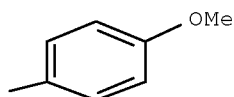


N

4
STEPS
→

PAGE 1-A





R
YIELD 45%

```

RX(22)      RCT  BM 837383-29-6
            RGT  AU 1333-74-0 H2
            PRO  M 870075-20-0
            CAT  12135-22-7 Pd(OH)2
            SOL  141-78-6 AcOEt

RX(3)       RCT  M 870075-20-0

            STAGE(1)
            RGT  E 144-55-8 NaHCO3, O 87413-09-0 Martin's reagent
            SOL  75-09-2 CH2Cl2
            CON  2.5 hours, room temperature

            STAGE(2)
            RGT  P 7772-98-7 Na2S2O3, E 144-55-8 NaHCO3
            SOL  7732-18-5 Water
            CON  room temperature

            PRO  N 853055-22-8

RX(20)      RCT  B 870074-98-9, BI 852049-56-0
            RGT  BK 534-17-8 Cs2CO3
            PRO  BJ 870075-18-6
            CAT  72287-26-4 Palladium, [1,1'-bis(diphenylphosphino-
            κP)ferrocene]dichloro-, (SP-4-2)-
            NTE  Suzuki coupling

RX(21)      RCT  BJ 870075-18-6
            RGT  W 7647-01-0 HCl
            PRO  I 870075-19-7
            SOL  7732-18-5 Water

RX(2)       RCT  I 870075-19-7

            STAGE(1)
            RGT  K 7553-56-2 I2, C 603-35-0 PPh3, D 288-32-4 1H-Imidazole

            STAGE(2)
            RCT  C 603-35-0
            RGT  L 121-44-8 Et3N
            CON  100 deg C

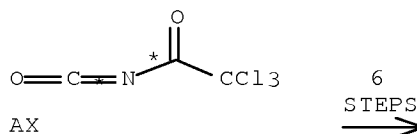
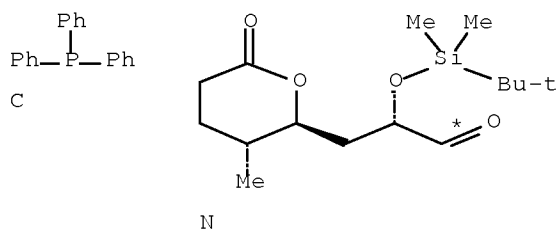
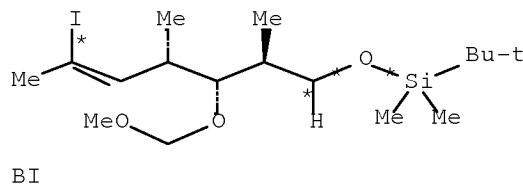
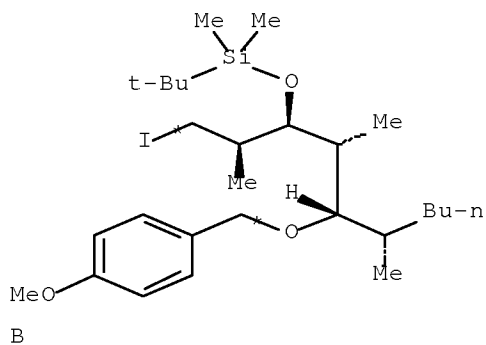
            PRO  J 870074-99-0
            NTE  Wittig salt formation in second stage, yield over 4 steps = 65%

RX(23)      RCT  J 870074-99-0, N 853055-22-8
            RGT  AI 917-54-4 MeLi

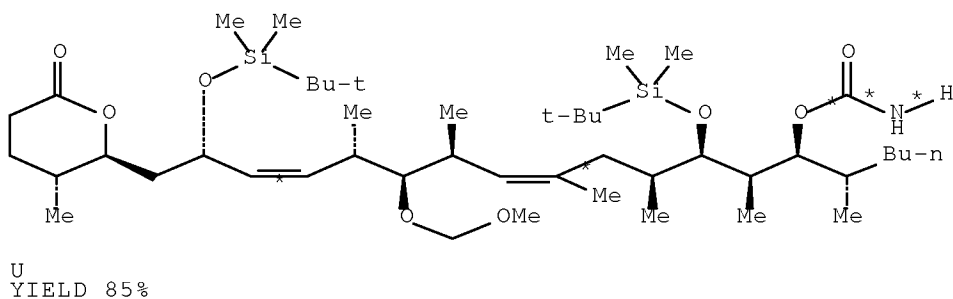
```

PRO R 870075-21-1
 NTE stereoselective, Wittig coupling

RX(155) OF 268 COMPOSED OF RX(20), RX(21), RX(2), RX(23), RX(4), RX(24)
 RX(155) E + EI + C + N + AX ==> U



6
 STEPS
 →



RX(20) RCT B 870074-98-9, BI 852049-56-0
 RGT BK 534-17-8 Cs2CO3
 PRO BJ 870075-18-6
 CAT 72287-26-4 Palladium, [1,1'-bis(diphenylphosphino-

κP)ferrocene]dichloro-, (SP-4-2)-
 NTE Suzuki coupling

RX(21) RCT BJ 870075-18-6
 RGT W 7647-01-0 HCl
 PRO I 870075-19-7
 SOL 7732-18-5 Water

RX(2) RCT I 870075-19-7

STAGE(1)
 RGT K 7553-56-2 I2, C 603-35-0 PPh3, D 288-32-4 1H-Imidazole

STAGE(2)
 RCT C 603-35-0
 RGT L 121-44-8 Et3N
 CON 100 deg C

PRO J 870074-99-0
 NTE Wittig salt formation in second stage, yield over 4 steps = 65%

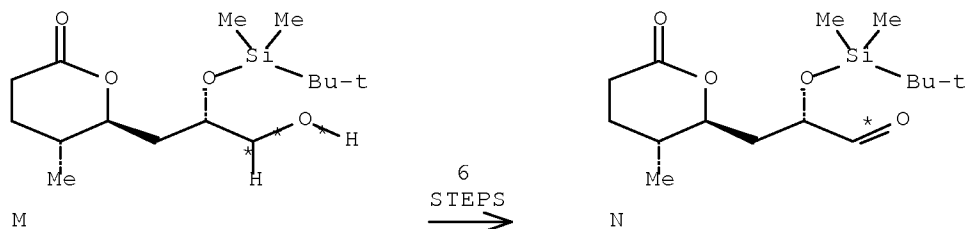
RX(23) RCT J 870074-99-0, N 853055-22-8
 RGT AI 917-54-4 MeLi
 PRO R 870075-21-1
 NTE stereoselective, Wittig coupling

RX(4) RCT R 870075-21-1
 RGT T 84-58-2 DDQ
 PRO S 870075-00-6
 NTE yield over 2 steps = 36%

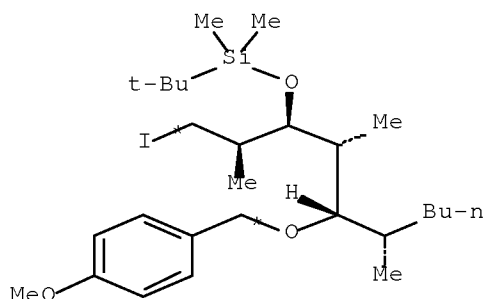
RX(24) RCT S 870075-00-6, AX 3019-71-4
 PRO U 870075-22-2
 NTE literature preparation

RX(156) OF 268 COMPOSED OF REACTION SEQUENCE RX(3), RX(23), RX(4), RX(24)
 AND REACTION SEQUENCE RX(20), RX(21), RX(2), RX(23), RX(4),

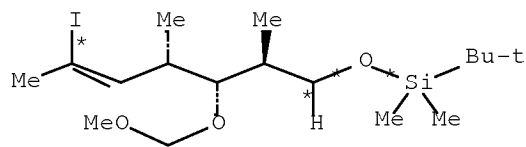
RX(24)
 ...M ==> N...
 ... E + BI + C + N + AX ==> U



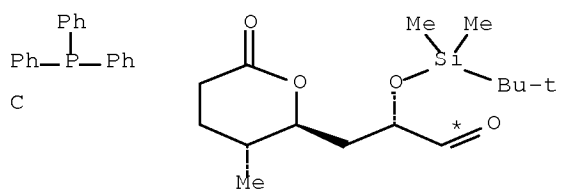
START NEXT REACTION SEQUENCE



B

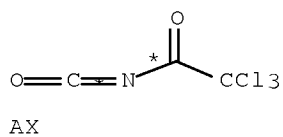


BI



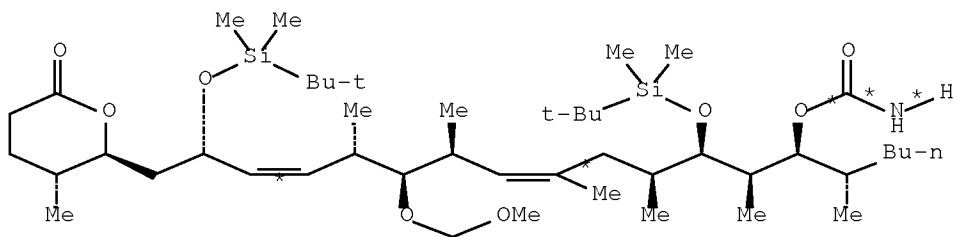
C

N



AX

6
STEPS
→



U
YIELD 85%

RX(3) RCT M 870075-20-0

STAGE(1)

RGT E 144-55-8 NaHCO₃, O 87413-09-0 Martin's reagent
SOL 75-09-2 CH₂Cl₂
CON 2.5 hours, room temperature

STAGE(2)

RGT P 7772-98-7 Na₂S₂O₃, E 144-55-8 NaHCO₃
SOL 7732-18-5 Water
CON room temperature

PRO N 853055-22-8

RX(20) RCT B ~~870074-98-9~~, BI ~~852049-56-0~~
 RGT BK 534-17-8 Cs2CO3
 PRO BJ 870075-18-6
 CAT 72287-26-4 Palladium, [1,1'-bis(diphenylphosphino-
 κP)ferrocene]dichloro-, (SP-4-2)-
 NTE Suzuki coupling

RX(21) RCT BJ 870075-18-6
 RGT W 7647-01-0 HCl
 PRO I 870075-19-7
 SOL 7732-18-5 Water

RX(2) RCT I 870075-19-7

STAGE(1)
 RGT K 7553-56-2 I2, C 603-35-0 PPh3, D 288-32-4 1H-Imidazole

STAGE(2)
 RCT C 603-35-0
 RGT L 121-44-8 Et3N
 CON 100 deg C

PRO J 870074-99-0
 NTE Wittig salt formation in second stage, yield over 4 steps = 65%

RX(23) RCT J 870074-99-0, N 853055-22-8
 RGT AI 917-54-4 MeLi
 PRO R 870075-21-1
 NTE stereoselective, Wittig coupling

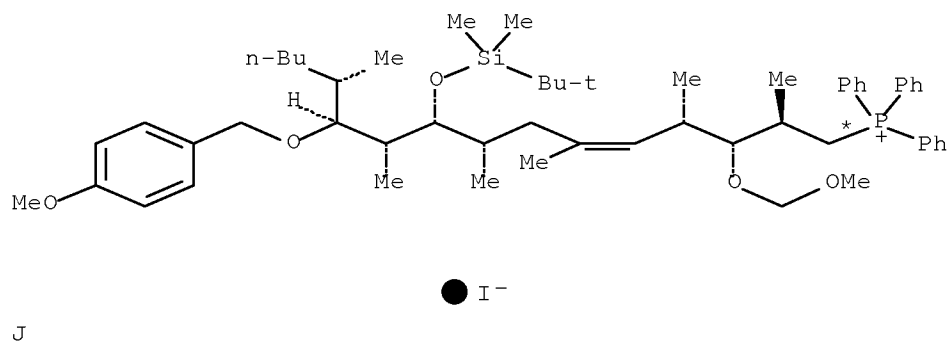
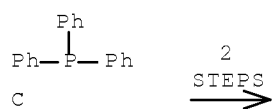
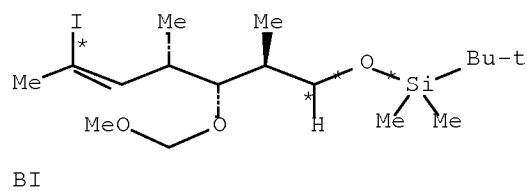
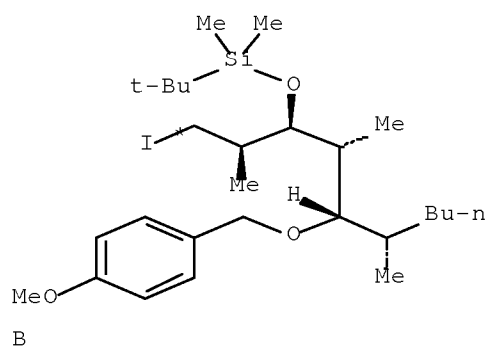
RX(4) RCT R 870075-21-1
 RGT T 84-58-2 DDQ
 PRO S 870075-00-6
 NTE yield over 2 steps = 36%

RX(24) RCT S 870075-00-6, AX 3019-71-4
 PRO U ~~870075-22-2~~
 NTE literature preparation

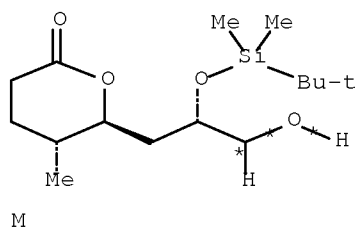
RX(164) OF 268 COMPOSED OF REACTION SEQUENCE RX(20), RX(21), RX(2), RX(23)
 AND REACTION SEQUENCE RX(3), RX(23)

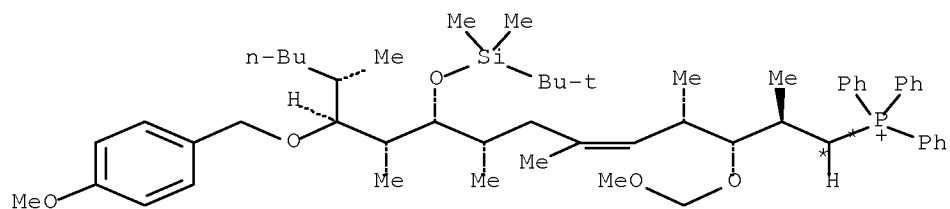
... B + BI + C ==> J...

...M + J ==> R



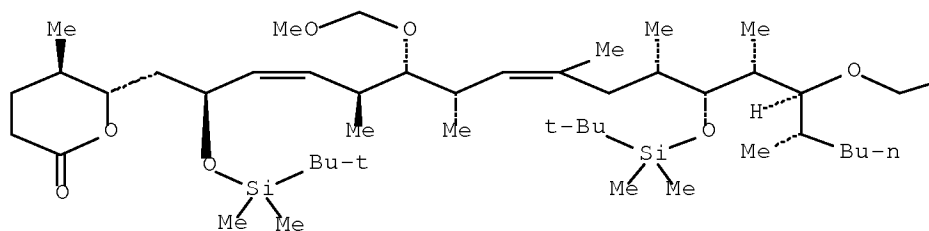
START NEXT REACTION SEQUENCE



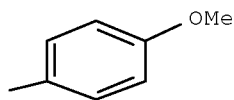


J

2
STEPS
→



PAGE 1-A



R
YIELD 45%

PAGE 1-B

RX(20)	RCT	B 870074-98-9, BI 852049-56-0
	RGT	BK 534-17-8 Cs ₂ CO ₃
	PRO	BJ 870075-18-6
	CAT	72287-26-4 Palladium, [1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-, (SP-4-2)-
	NTE	Suzuki coupling
RX(21)	RCT	BJ 870075-18-6

RGT W 7647-01-0 HCl
PRO I 870075-19-7
SOL 7732-18-5 Water

RX(2) RCT I 870075-19-7

STAGE(1)

RGT K 7553-56-2 I2, C 603-35-0 PPh3, D 288-32-4 1H-Imidazole

STAGE(2)

RCT C 603-35-0

RGT L 121-44-8 Et3N

CON 100 deg C

PRO J 870074-99-0

NTE Wittig salt formation in second stage, yield over 4 steps = 65%

RX(3) RCT M 870075-20-0

STAGE(1)

RGT E 144-55-8 NaHCO3, O 87413-09-0 Martin's reagent

SOL 75-09-2 CH2Cl2

CON 2.5 hours, room temperature

STAGE(2)

RGT P 7772-98-7 Na2S2O3, E 144-55-8 NaHCO3

SOL 7732-18-5 Water

CON room temperature

PRO N 853055-22-8

RX(23) RCT J 870074-99-0, N 853055-22-8

RGT AI 917-54-4 MeLi

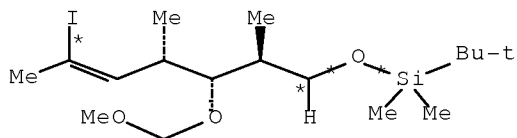
PRO R 870075-21-1

NTE stereoselective, Wittig coupling

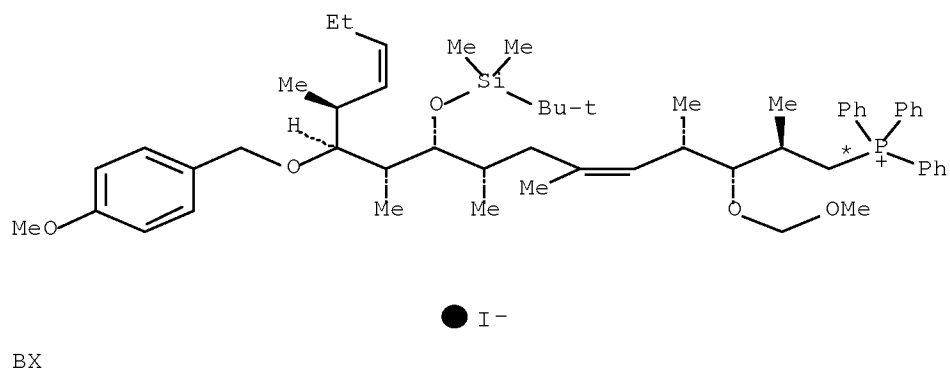
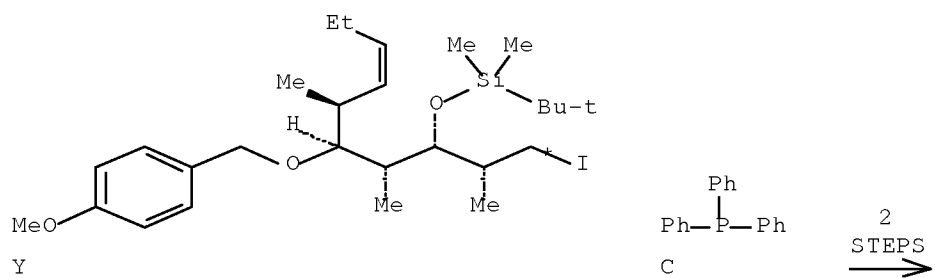
RX(165) OF 268 COMPOSED OF REACTION SEQUENCE RX(27), RX(28), RX(29), RX(30)
AND REACTION SEQUENCE RX(3), RX(30)

... BI + Y + C ==> BX...

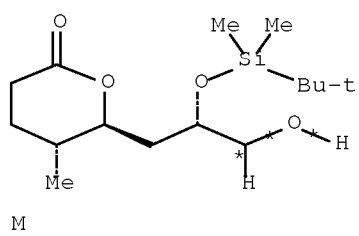
...M + BX ==> BY

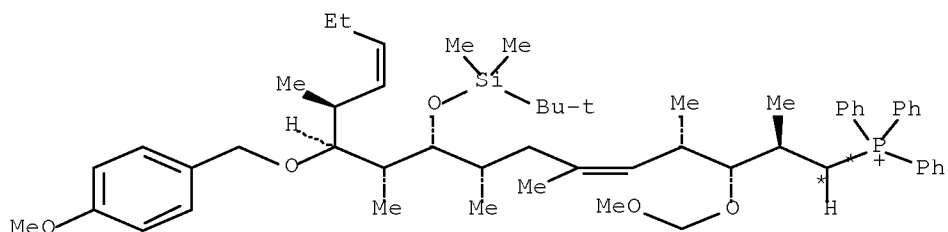


BI



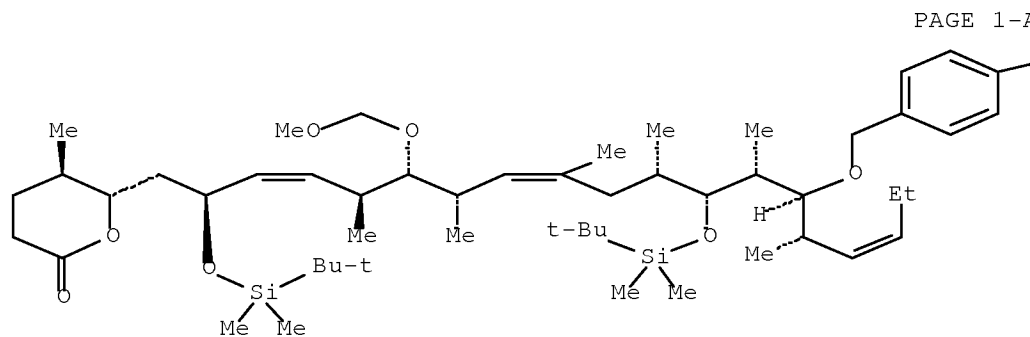
START NEXT REACTION SEQUENCE





BX

2
STEPS
→



PAGE 1-A

OMe

BY
YIELD 50%

PAGE 1-B

RX(27) RCT BI 852049-56-0, Y 870075-02-8
RGT BK 534-17-8 Cs2CO3
PRO BV 870075-26-6
CAT 72287-26-4 Palladium, [1,1'-bis(diphenylphosphino-
κP)ferrocene]dichloro-, (SP-4-2)-
NTE Suzuki coupling

RX(28) RCT BV 870075-26-6
 RGT W 7647-01-0 HCl
 PRO BW 870075-27-7
 SOL 7732-18-5 Water
 NTE regioselective

RX(29) RCT BW 870075-27-7

 STAGE(1)
 RGT K 7553-56-2 I2, C 603-35-0 PPh3, D 288-32-4 1H-Imidazole

 STAGE(2)
 RCT C 603-35-0
 RGT L 121-44-8 Et3N
 CON 100 deg C

 PRO BX 870075-28-8
 NTE stereoselective, Wittig salt formation in second stage

RX(3) RCT M 870075-20-0

 STAGE(1)
 RGT E 144-55-8 NaHCO3, O 87413-09-0 Martin's reagent
 SOL 75-09-2 CH2Cl2
 CON 2.5 hours, room temperature

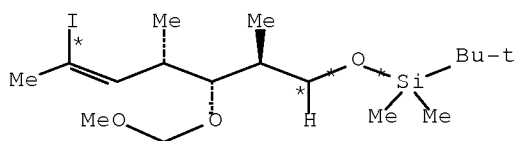
 STAGE(2)
 RGT P 7772-98-7 Na2S2O3, E 144-55-8 NaHCO3
 SOL 7732-18-5 Water
 CON room temperature

 PRO N 853055-22-8

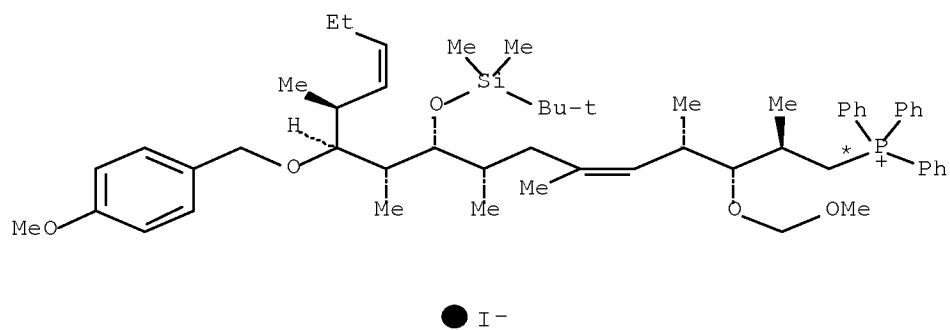
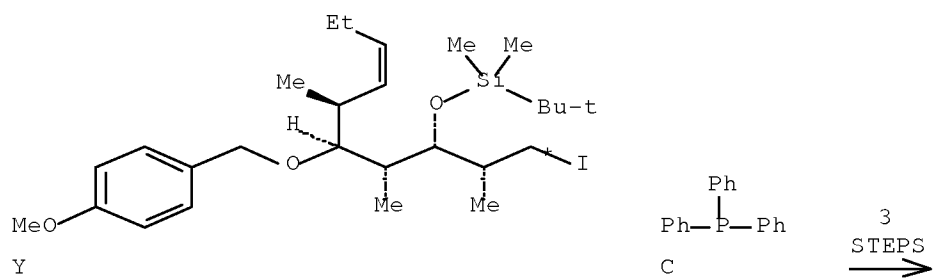
RX(30) RCT N 853055-22-8, BX 870075-28-8
 RGT AU 1333-74-0 H2
 PRO BY 870075-29-9
 CAT 12135-22-7 Pd(OH)2
 SOL 141-78-6 AcOEt
 NTE Wittig coupling

RX(174) OF 268 COMPOSED OF REACTION SEQUENCE RX(27), RX(28), RX(29), RX(30)
 AND REACTION SEQUENCE RX(22), RX(3), RX(30)

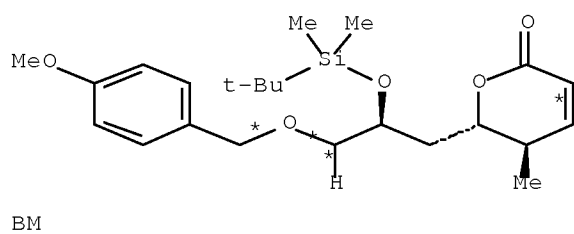
... BI + Y + C ==> BX...
 ...BM + BX ==> BY

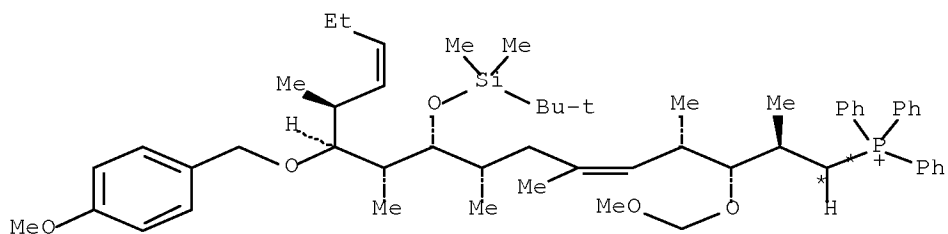


BI



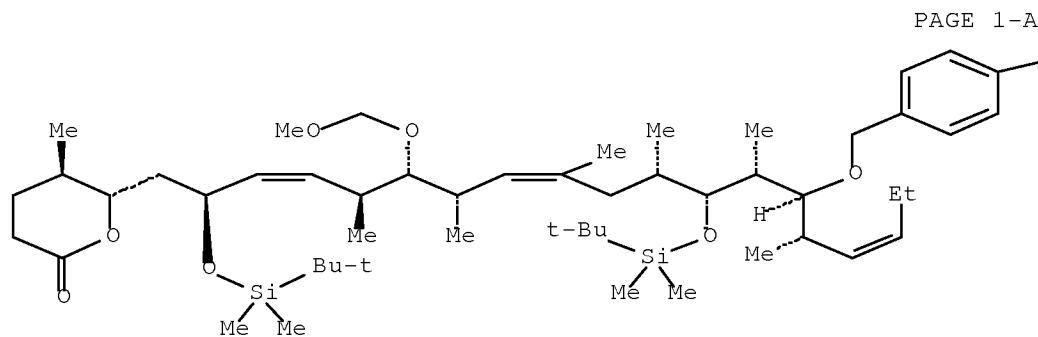
START NEXT REACTION SEQUENCE





BX

3
STEPS
→



PAGE 1-A

OMe

BY
YIELD 50%

PAGE 1-B

RX(27) RCT BI 852049-56-0, Y 870075-02-8
 RGT BK 534-17-8 Cs₂CO₃
 PRO BV 870075-26-6
 CAT 72287-26-4 Palladium, [1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-, (SP-4-2)-
 NTE Suzuki coupling

RX(28) RCT BV 870075-26-6
 RGT W 7647-01-0 HCl
 PRO BW 870075-27-7
 SOL 7732-18-5 Water
 NTE regioselective

RX(29) RCT BW 870075-27-7

 STAGE(1)
 RGT K 7553-56-2 I2, C 603-35-0 PPh3, D 288-32-4 1H-Imidazole

 STAGE(2)
 RCT C 603-35-0
 RGT L 121-44-8 Et3N
 CON 100 deg C

 PRO BX 870075-28-8
 NTE stereoselective, Wittig salt formation in second stage

RX(22) RCT BM 837383-29-6
 RGT AU 1333-74-0 H2
 PRO M 870075-20-0
 CAT 12135-22-7 Pd(OH)2
 SOL 141-78-6 AcOEt

RX(3) RCT M 870075-20-0

 STAGE(1)
 RGT E 144-55-8 NaHCO3, O 87413-09-0 Martin's reagent
 SOL 75-09-2 CH2Cl2
 CON 2.5 hours, room temperature

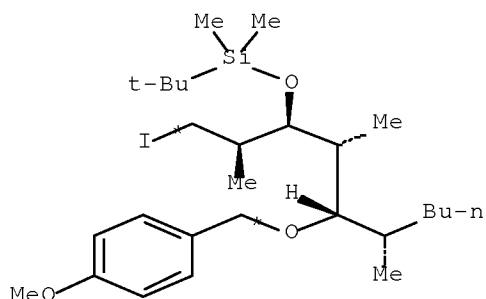
 STAGE(2)
 RGT P 7772-98-7 Na2S2O3, E 144-55-8 NaHCO3
 SOL 7732-18-5 Water
 CON room temperature

 PRO N 853055-22-8

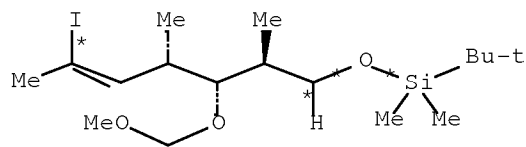
RX(30) RCT N 853055-22-8, BX 870075-28-8
 RGT AU 1333-74-0 H2
 PRO BY 870075-29-9
 CAT 12135-22-7 Pd(OH)2
 SOL 141-78-6 AcOEt
 NTE Wittig coupling

RX(190) OF 268 COMPOSED OF RX(20), RX(21), RX(2), RX(23), RX(4)

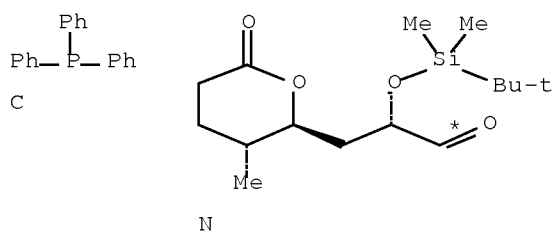
RX(190) E + BI + C + N ==> S



B



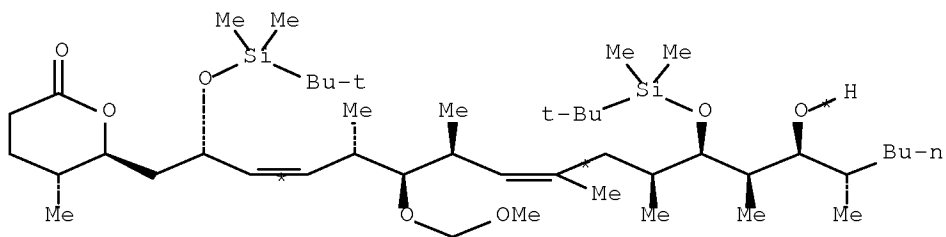
BI



C

N

5
STEPS
→



S
YIELD 80%

RX(20)	RCT	B 870074-98-9, BI 852049-56-0
	RGT	BK 534-17-8 Cs ₂ CO ₃
	PRO	BJ 870075-18-6
	CAT	72287-26-4 Palladium, [1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-, (SP-4-2)-
	NTE	Suzuki coupling
RX(21)	RCT	BJ 870075-18-6
	RGT	W 7647-01-0 HCl
	PRO	I 870075-19-7
	SOL	7732-18-5 Water

RX(2) RCT I 870075-19-7

STAGE(1)

RGT K 7553-56-2 I2, C 603-35-0 PPh3, D 288-32-4 1H-Imidazole

STAGE(2)

RCT C 603-35-0

RGT L 121-44-8 Et3N

CON 100 deg C

PRO J 870074-99-0

NTE Wittig salt formation in second stage, yield over 4 steps = 65%

RX(23) RCT J 870074-99-0, N 853055-22-8

RGT AI 917-54-4 MeLi

PRO R 870075-21-1

NTE stereoselective, Wittig coupling

RX(4) RCT R 870075-21-1

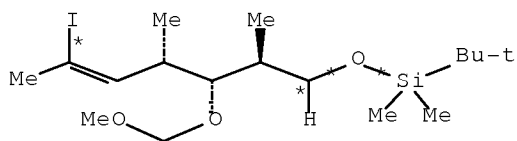
RGT T 84-58-2 DDQ

PRO S 870075-00-6

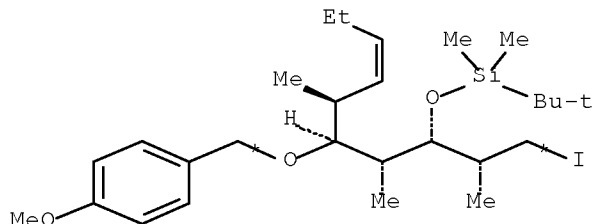
NTE yield over 2 steps = 36%

RX(201) OF 268 COMPOSED OF RX(27), RX(28), RX(29), RX(30), RX(31)

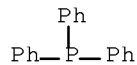
RX(201) BI + Y + C + N ==> BZ



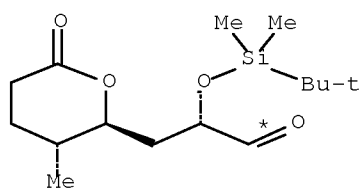
BI



Y

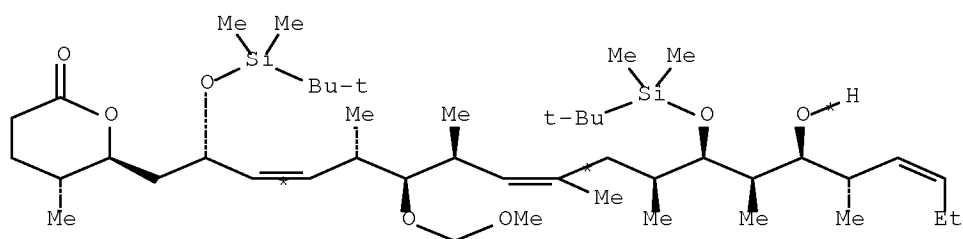


C



N

5
STEPS
→



BZ
YIELD 93%

RX(27) RCT BI 852049-56-0, Y 870075-02-8
RGT BK 534-17-8 Cs₂CO₃
PRO BV 870075-26-6
CAT 72287-26-4 Palladium, [1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-, (SP-4-2)-
NTE Suzuki coupling

RX(28) RCT BV 870075-26-6
RGT W 7647-01-0 HCl
PRO BW 870075-27-7
SOL 7732-18-5 Water
NTE regioselective

RX(29) RCT BW 870075-27-7

STAGE(1)

RGT K 7553-56-2 I₂, C 603-35-0 PPh₃, D 288-32-4 1H-Imidazole

STAGE(2)

RCT C 603-35-0
RGT L 121-44-8 Et₃N
CON 100 deg C

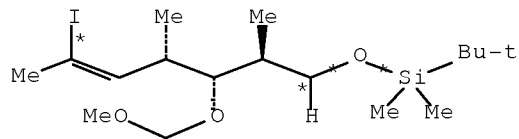
PRO BX 870075-28-8
NTE stereoselective, Wittig salt formation in second stage

RX(30) RCT N 853055-22-8, BX 870075-28-8
RGT AU 1333-74-0 H₂
PRO BY 870075-29-9
CAT 12135-22-7 Pd(OH)₂

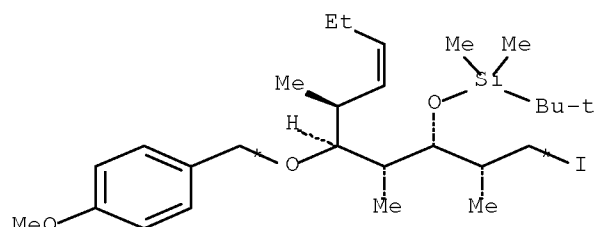
SOL 141-78-6 AcOEt
 NTE Wittig coupling

RX(31) RCT BY 870075-29-9
 RGT T 84-58-2 DDQ
 PRO BZ 870075-30-2

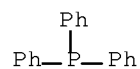
RX(209) OF 268 COMPOSED OF RX(27), RX(28), RX(29), RX(30), RX(31), RX(32)
 RX(209) BI + Y + C + N + AX ==> Z



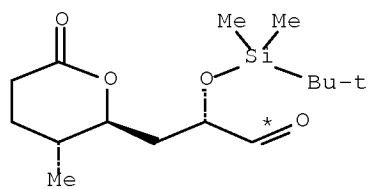
BI



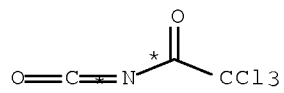
Y



C

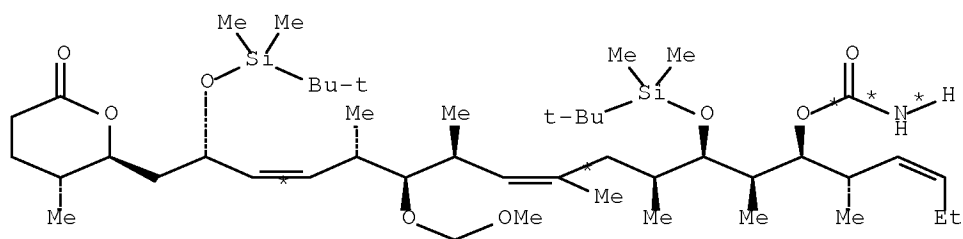


N



AX

6
 STEPS
 →



Z
YIELD 79%

RX(27) RCT BI 852049-56-0, Y 870075-02-8
 RGT BK 534-17-8 Cs₂CO₃
 PRO BV 870075-26-6
 CAT 72287-26-4 Palladium, [1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-, (SP-4-2)-
 NTE Suzuki coupling

RX(28) RCT BV 870075-26-6
 RGT W 7647-01-0 HCl
 PRO BW 870075-27-7
 SOL 7732-18-5 Water
 NTE regioselective

RX(29) RCT BW 870075-27-7

STAGE(1)
 RGT K 7553-56-2 I₂, C 603-35-0 PPh₃, D 288-32-4 1H-Imidazole

STAGE(2)
 RCT C 603-35-0
 RGT L 121-44-8 Et₃N
 CON 100 deg C

PRO BX 870075-28-8
 NTE stereoselective, Wittig salt formation in second stage

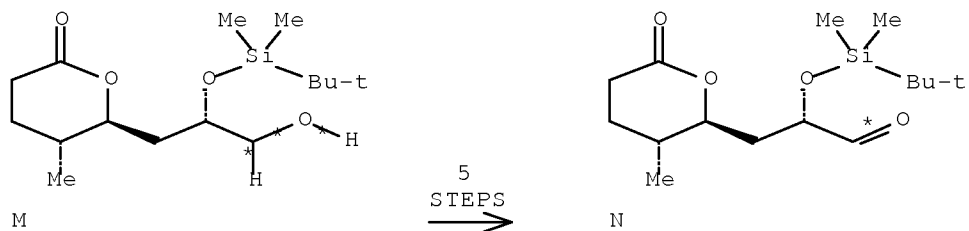
RX(30) RCT N 853055-22-8, BX 870075-28-8
 RGT AU 1333-74-0 H₂
 PRO BY 870075-29-9
 CAT 12135-22-7 Pd(OH)₂
 SOL 141-78-6 AcOEt
 NTE Wittig coupling

RX(31) RCT BY 870075-29-9
 RGT T 84-58-2 DDQ
 PRO BZ 870075-30-2

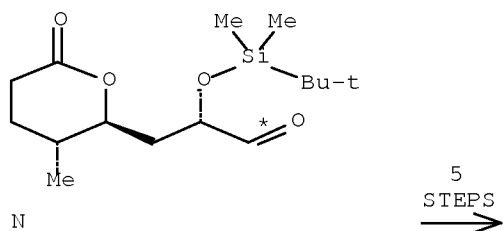
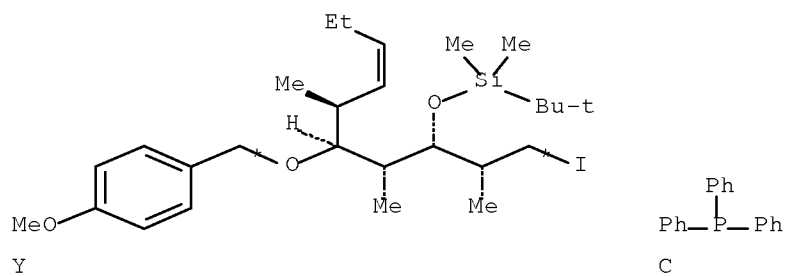
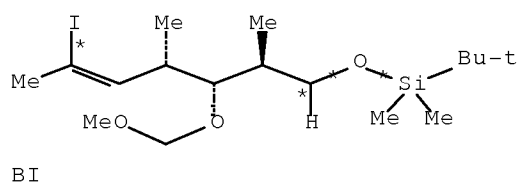
RX(32) RCT BZ 870075-30-2, AX 3019-71-4
 PRO Z 870075-31-3
 NTE literature preparation

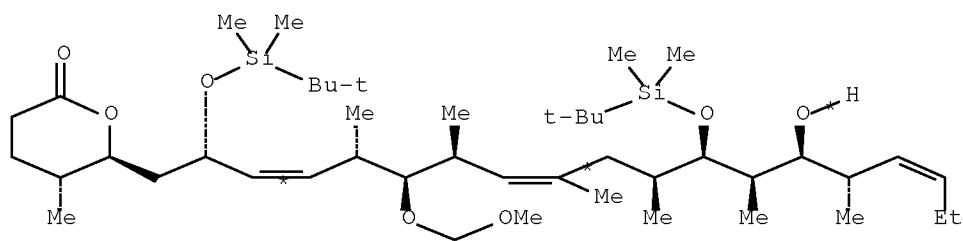
RX(217) OF 268 COMPOSED OF REACTION SEQUENCE RX(3), RX(30), RX(31)
 AND REACTION SEQUENCE RX(27), RX(28), RX(29), RX(30), RX(31)

...M ==> N...
 ... BI + Y + C + N ==> BZ



START NEXT REACTION SEQUENCE





BZ
YIELD 93%

RX(3) RCT M 870075-20-0

STAGE(1)

RGT E 144-55-8 NaHCO₃, O 87413-09-0 Martin's reagent
SOL 75-09-2 CH₂Cl₂
CON 2.5 hours, room temperature

STAGE(2)

RGT P 7772-98-7 Na₂S₂O₃, E 144-55-8 NaHCO₃
SOL 7732-18-5 Water
CON room temperature

PRO N 853055-22-8

RX(27) RCT BI 852049-56-0, Y 870075-02-8
RGT BK 534-17-8 Cs₂CO₃
PRO BV 870075-26-6
CAT 72287-26-4 Palladium, [1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-, (SP-4-2)-
NTE Suzuki coupling

RX(28) RCT BV 870075-26-6
RGT W 7647-01-0 HCl
PRO BW 870075-27-7
SOL 7732-18-5 Water
NTE regioselective

RX(29) RCT BW 870075-27-7

STAGE(1)

RGT K 7553-56-2 I₂, C 603-35-0 PPh₃, D 288-32-4 1H-Imidazole

STAGE(2)

RCT C 603-35-0
RGT L 121-44-8 Et₃N
CON 100 deg C

PRO BX 870075-28-8
NTE stereoselective, Wittig salt formation in second stage

RX(30) RCT N 853055-22-8, BX 870075-28-8
RGT AU 1333-74-0 H₂
PRO BY 870075-29-9
CAT 12135-22-7 Pd(OH)₂

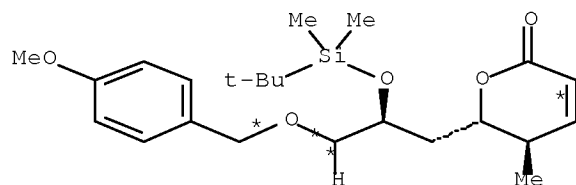
SOL 141-78-6 AcOEt
 NTE Wittig coupling

RX(31) RCT BY 870075-29-9
 RGT T 84-58-2 DDQ
 PRO BZ 870075-30-2

RX(218) OF 268 COMPOSED OF REACTION SEQUENCE RX(22), RX(3), RX(30), RX(31)
 AND REACTION SEQUENCE RX(27), RX(28), RX(29), RX(30), RX(31)

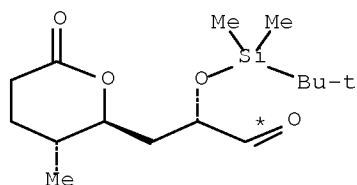
...BM ==> N...

... BI + Y + C + N ==> BZ



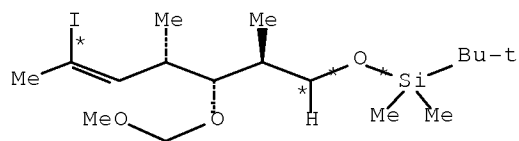
BM

5
 STEPS
 →

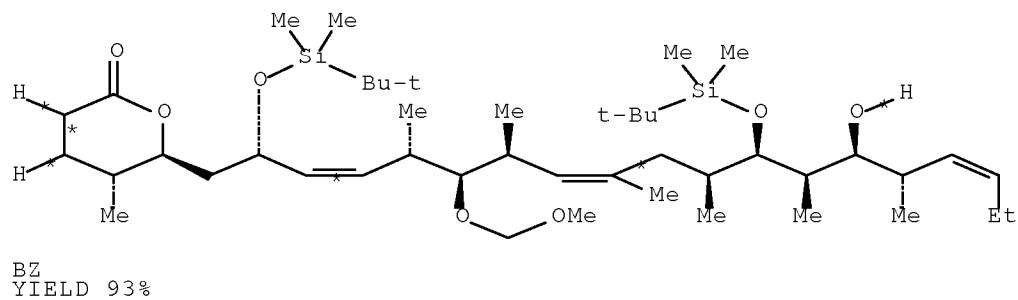
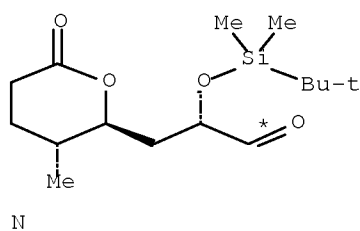
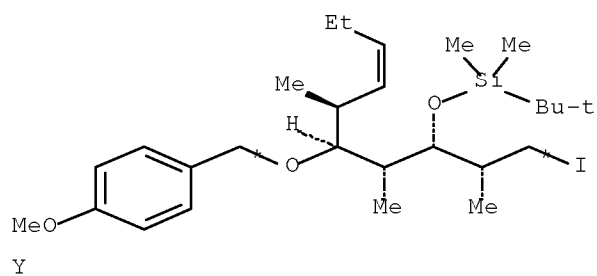


N

START NEXT REACTION SEQUENCE



BI



RX(22) RCT BM 837383-29-6
 RGT AU 1333-74-0 H2
 PRO M 870075-20-0
 CAT 12135-22-7 Pd(OH)2
 SOL 141-78-6 AcOEt

RX(3) RCT M 870075-20-0

STAGE(1)

 RGT E 144-55-8 NaHCO3, O 87413-09-0 Martin's reagent
 SOL 75-09-2 CH2Cl2
 CON 2.5 hours, room temperature

STAGE(2)

RGT P 7772-98-7 Na2S2O3, E 144-55-8 NaHCO3
 SOL 7732-18-5 Water
 CON room temperature

PRO N 853055-22-8

RX(27) RCT BI 852049-56-0, Y 870075-02-8
 RGT BK 534-17-8 Cs2CO3
 PRO BV 870075-26-6
 CAT 72287-26-4 Palladium, [1,1'-bis(diphenylphosphino-
 κP)ferrocene]dichloro-, (SP-4-2)-
 NTE Suzuki coupling

RX(28) RCT BV 870075-26-6
 RGT W 7647-01-0 HCl
 PRO BW 870075-27-7
 SOL 7732-18-5 Water
 NTE regioselective

RX(29) RCT BW 870075-27-7

STAGE(1)

RGT K 7553-56-2 I2, C 603-35-0 PPh3, D 288-32-4 1H-Imidazole

STAGE(2)

RCT C 603-35-0
 RGT L 121-44-8 Et3N
 CON 100 deg C

PRO BX 870075-28-8
 NTE stereoselective, Wittig salt formation in second stage

RX(30) RCT N 853055-22-8, BX 870075-28-8
 RGT AU 1333-74-0 H2
 PRO BY 870075-29-9
 CAT 12135-22-7 Pd(OH)2
 SOL 141-78-6 AcOEt
 NTE Wittig coupling

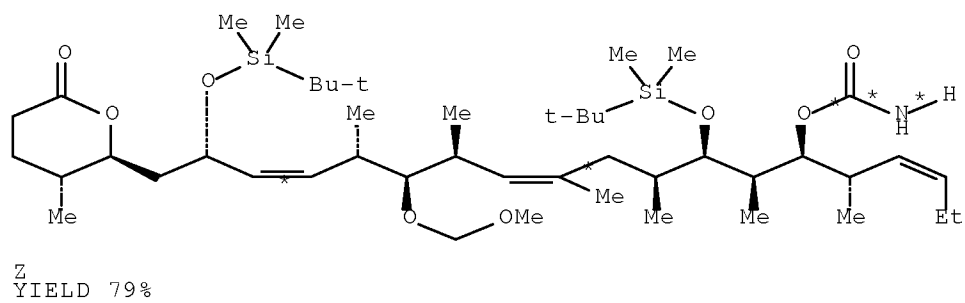
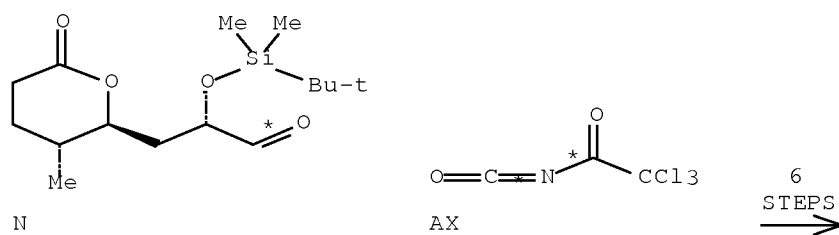
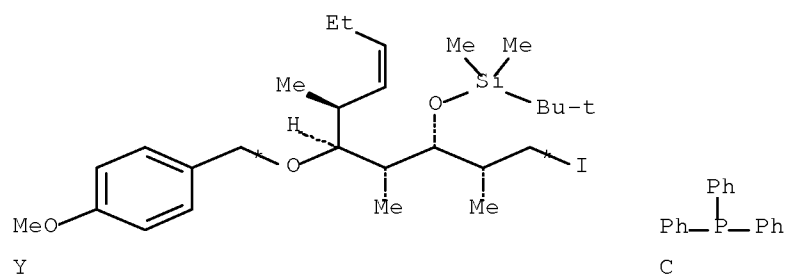
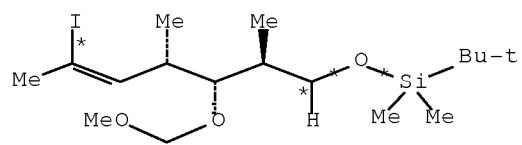
RX(31) RCT BY 870075-29-9
 RGT T 84-58-2 DDQ
 PRO BZ 870075-30-2

RX(219) OF 268 COMPOSED OF REACTION SEQUENCE RX(3), RX(30), RX(31), RX(32)
 AND REACTION SEQUENCE RX(27), RX(28), RX(29), RX(30), RX(31),
 RX(32)

...M ==> N...
 ... BI + Y + C + N + AX ==> Z



START NEXT REACTION SEQUENCE



RX(3) RCT M 870075-20-0

STAGE(1)
 RGT E 144-55-8 NaHCO₃, O 87413-09-0 Martin's reagent
 SOL 75-09-2 CH₂Cl₂
 CON 2.5 hours, room temperature

STAGE(2)
 RGT P 7772-98-7 Na₂S₂O₃, E 144-55-8 NaHCO₃
 SOL 7732-18-5 Water
 CON room temperature

PRO N 853055-22-8

RX(27) RCT BI 852049-56-0, Y 870075-02-8
 RGT BK 534-17-8 Cs₂CO₃
 PRO BV 870075-26-6
 CAT 72287-26-4 Palladium, [1,1'-bis(diphenylphosphino-
 κP)ferrocene]dichloro-, (SP-4-2)-
 NTE Suzuki coupling

RX(28) RCT BV 870075-26-6
 RGT W 7647-01-0 HCl
 PRO BW 870075-27-7
 SOL 7732-18-5 Water
 NTE regioselective

RX(29) RCT BW 870075-27-7

STAGE(1)
 RGT K 7553-56-2 I₂, C 603-35-0 PPh₃, D 288-32-4 1H-Imidazole

STAGE(2)
 RCT C 603-35-0
 RGT L 121-44-8 Et₃N
 CON 100 deg C

PRO BX 870075-28-8
 NTE stereoselective, Wittig salt formation in second stage

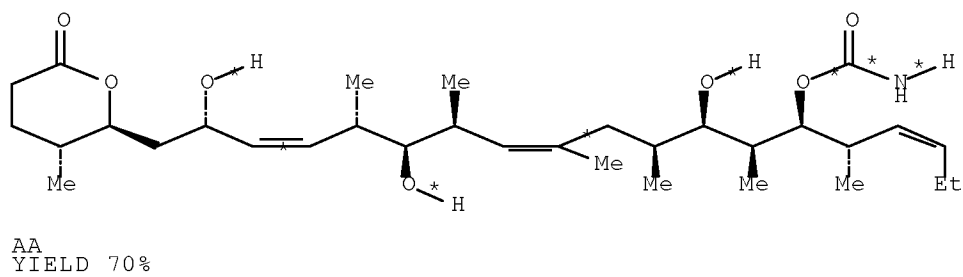
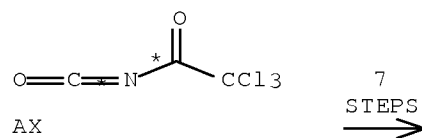
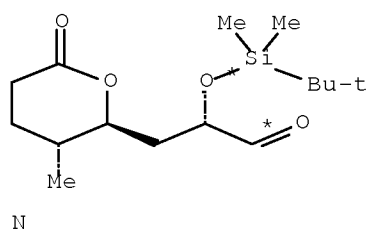
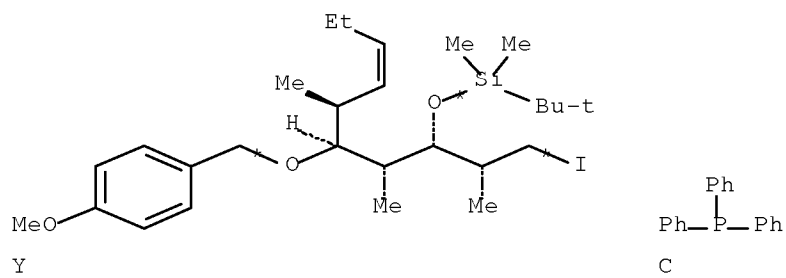
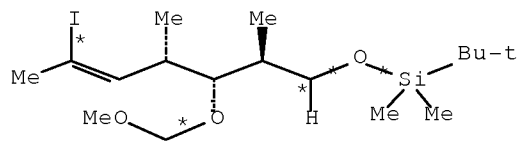
RX(30) RCT N 853055-22-8, BX 870075-28-8
 RGT AU 1333-74-0 H₂
 PRO BY 870075-29-9
 CAT 12135-22-7 Pd(OH)₂
 SOL 141-78-6 AcOEt
 NTE Wittig coupling

RX(31) RCT BY 870075-29-9
 RGT T 84-58-2 DDQ
 PRO BZ 870075-30-2

RX(32) RCT BZ 870075-30-2, AX 3019-71-4
 PRO Z 870075-31-3
 NTE literature preparation

RX(220) OF 268 COMPOSED OF RX(27), RX(28), RX(29), RX(30), RX(31), RX(32),
 RX(7)

RX(220) BI + Y + C + N + AX ==> AA



RX(27) RCT BI 852049-56-0, Y 870075-02-8
RGT BK 534-17-8 Cs2CO3

PRO BV 870075-26-6
CAT 72287-26-4 Palladium, [1,1'-bis(diphenylphosphino-
κP)ferrocene]dichloro-, (SP-4-2)-
NTE Suzuki coupling

RX(28) RCT BV 870075-26-6
RGT W 7647-01-0 HCl
PRO BW 870075-27-7
SOL 7732-18-5 Water
NTE regioselective

RX(29) RCT BW 870075-27-7

STAGE(1)

RGT K 7553-56-2 I2, C 603-35-0 PPh3, D 288-32-4 1H-Imidazole

STAGE(2)

RCT C 603-35-0
RGT L 121-44-8 Et3N
CON 100 deg C

PRO BX 870075-28-8
NTE stereoselective, Wittig salt formation in second stage

RX(30) RCT N 853055-22-8, BX 870075-28-8
RGT AU 1333-74-0 H2
PRO BY 870075-29-9
CAT 12135-22-7 Pd(OH)2
SOL 141-78-6 AcOEt
NTE Wittig coupling

RX(31) RCT BY 870075-29-9
RGT T 84-58-2 DDQ
PRO BZ 870075-30-2

RX(32) RCT BZ 870075-30-2, AX 3019-71-4
PRO Z 870075-31-3
NTE literature preparation

RX(7) RCT Z 870075-31-3
RGT W 7647-01-0 HCl
PRO AA 870075-03-9
SOL 7732-18-5 Water
NTE yield over 8 steps = 17%

RX(236) OF 268 COMPOSED OF REACTION SEQUENCE RX(3), RX(23), RX(4), RX(24),
RX(5)

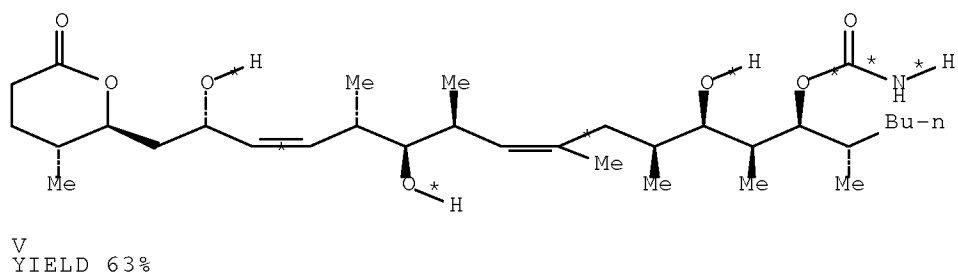
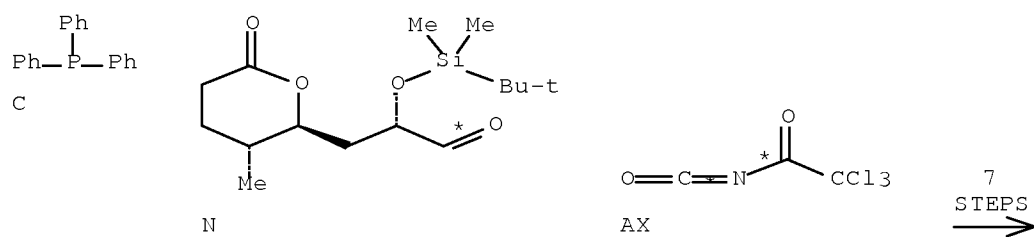
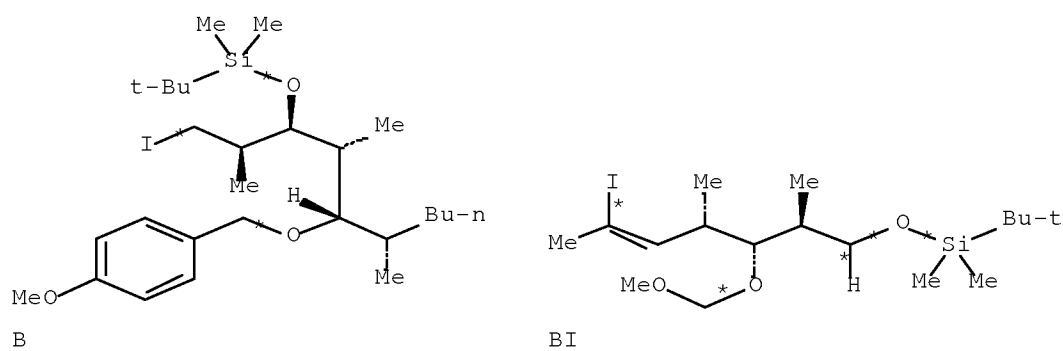
AND REACTION SEQUENCE RX(20), RX(21), RX(2), RX(23), RX(4),
RX(24), RX(5)

...M ==> N...

... E + EI + C + N + AX ==> V



START NEXT REACTION SEQUENCE



RX(3) RCT M 870075-20-0

STAGE(1)
 RGT E 144-55-8 NaHCO₃, O 87413-09-0 Martin's reagent
 SOL 75-09-2 CH₂Cl₂
 CON 2.5 hours, room temperature

STAGE(2)
 RGT P 7772-98-7 Na₂S₂O₃, E 144-55-8 NaHCO₃
 SOL 7732-18-5 Water
 CON room temperature

PRO N 853055-22-8

RX(20) RCT B 870074-98-9, BI 852049-56-0
 RGT BK 534-17-8 Cs₂CO₃
 PRO BJ 870075-18-6
 CAT 72287-26-4 Palladium, [1,1'-bis(diphenylphosphino-
 κP)ferrocene]dichloro-, (SP-4-2)-
 NTE Suzuki coupling

RX(21) RCT BJ 870075-18-6
 RGT W 7647-01-0 HCl
 PRO I 870075-19-7
 SOL 7732-18-5 Water

RX(2) RCT I 870075-19-7

STAGE(1)
 RGT K 7553-56-2 I₂, C 603-35-0 PPh₃, D 288-32-4 1H-Imidazole

STAGE(2)
 RCT C 603-35-0
 RGT L 121-44-8 Et₃N
 CON 100 deg C

PRO J 870074-99-0
 NTE Wittig salt formation in second stage, yield over 4 steps = 65%

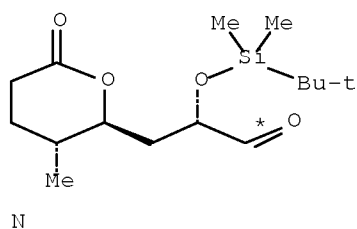
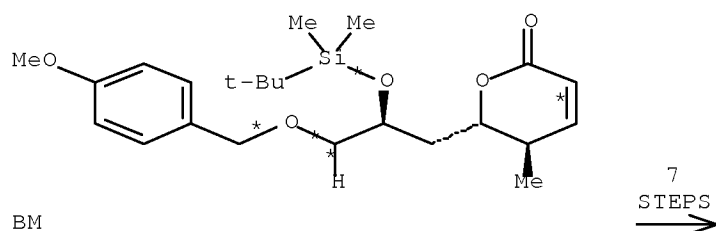
RX(23) RCT J 870074-99-0, N 853055-22-8
 RGT AI 917-54-4 MeLi
 PRO R 870075-21-1
 NTE stereoselective, Wittig coupling

RX(4) RCT R 870075-21-1
 RGT T 84-58-2 DDQ
 PRO S 870075-00-6
 NTE yield over 2 steps = 36%

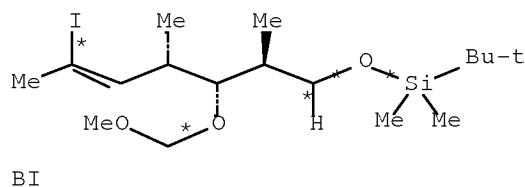
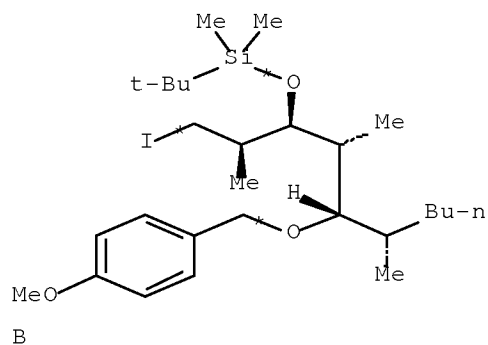
RX(24) RCT S 870075-00-6, AX 3019-71-4
 PRO U 870075-22-2
 NTE literature preparation

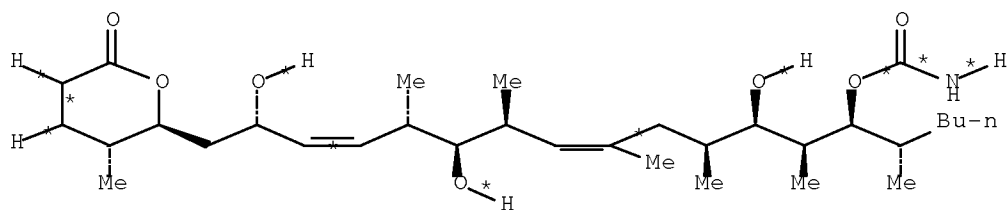
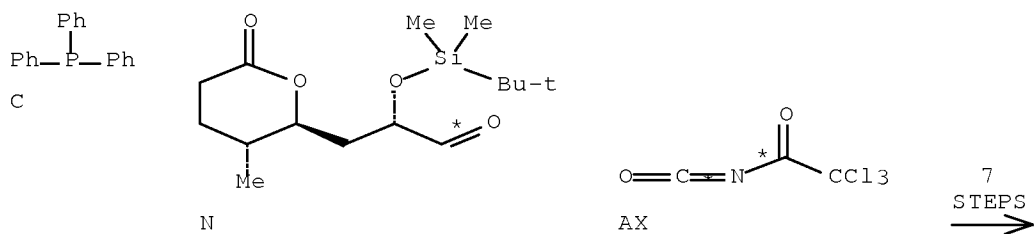
RX(5) RCT U 870075-22-2
 RGT W 7647-01-0 HCl
 PRO V 870075-01-7
 SOL 7732-18-5 Water
 NTE yield over 2 steps = 54%

RX(237) OF 268 COMPOSED OF REACTION SEQUENCE RX(22), RX(3), RX(23), RX(4),
 RX(24), RX(5)
 AND REACTION SEQUENCE RX(20), RX(21), RX(2), RX(23), RX(4),
 RX(24), RX(5)
 ...BM ==> N...
 ... B + BI + C + N + AX ==> V



START NEXT REACTION SEQUENCE





RX(22) RCT BM 837383-29-6
 RGT AU 1333-74-0 H2
 PRO M 870075-20-0
 CAT 12135-22-7 Pd(OH)2
 SOL 141-78-6 AcOEt

RX(3) RCT M 870075-20-0

STAGE(1)

RGT E 144-55-8 NaHCO3, O 87413-09-0 Martin's reagent
 SOL 75-09-2 CH2Cl2
 CON 2.5 hours, room temperature

STAGE(2)

RGT P 7772-98-7 Na2S2O3, E 144-55-8 NaHCO3
 SOL 7732-18-5 Water
 CON room temperature

PRO N 853055-22-8

RX(20) RCT B 870074-98-9, BI 852049-56-0
 RGT BK 534-17-8 Cs2CO3
 PRO BJ 870075-18-6
 CAT 72287-26-4 Palladium, [1,1'-bis(diphenylphosphino-
 κP)ferrocene]dichloro-, (SP-4-2)-
 NTE Suzuki coupling

RX(21) RCT BJ 870075-18-6
 RGT W 7647-01-0 HCl
 PRO I 870075-19-7
 SOL 7732-18-5 Water

RX(2) RCT I 870075-19-7

STAGE(1)
RGT K 7553-56-2 I2, C 603-35-0 PPh3, D 288-32-4 1H-Imidazole

STAGE(2)
RCT C 603-35-0
RGT L 121-44-8 Et3N
CON 100 deg C

PRO J 870074-99-0
NTE Wittig salt formation in second stage, yield over 4 steps = 65%

RX(23) RCT J 870074-99-0, N 853055-22-8
RGT AI 917-54-4 MeLi
PRO R 870075-21-1
NTE stereoselective, Wittig coupling

RX(4) RCT R 870075-21-1
RGT T 84-58-2 DDQ
PRO S 870075-00-6
NTE yield over 2 steps = 36%

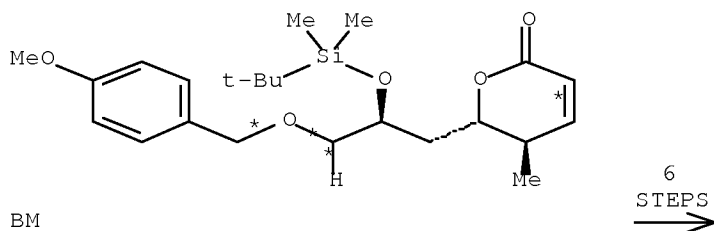
RX(24) RCT S 870075-00-6, AX 3019-71-4
PRO U 870075-22-2
NTE literature preparation

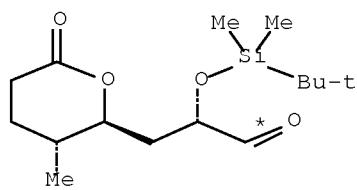
RX(5) RCT U 870075-22-2
RGT W 7647-01-0 HCl
PRO V ~~870075-01-7~~
SOL 7732-18-5 Water
NTE yield over 2 steps = 54%

RX(238) OF 268 COMPOSED OF REACTION SEQUENCE RX(22), RX(3), RX(23), RX(4),
RX(24)
AND REACTION SEQUENCE RX(20), RX(21), RX(2), RX(23), RX(4),
RX(24)

...BM ==> N...

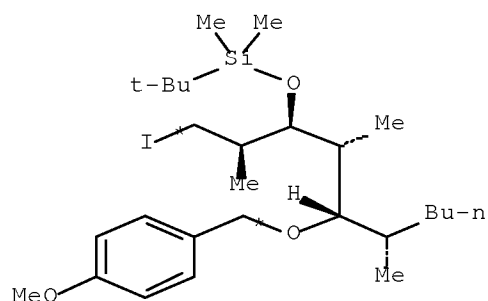
... E + SI + C + N + AX ==> U



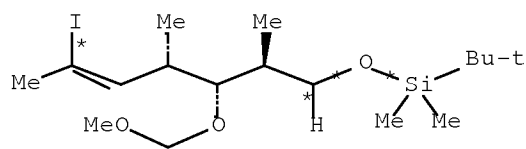


N

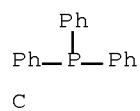
START NEXT REACTION SEQUENCE



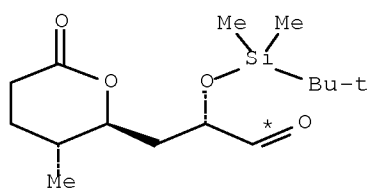
B



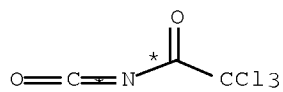
BI



C

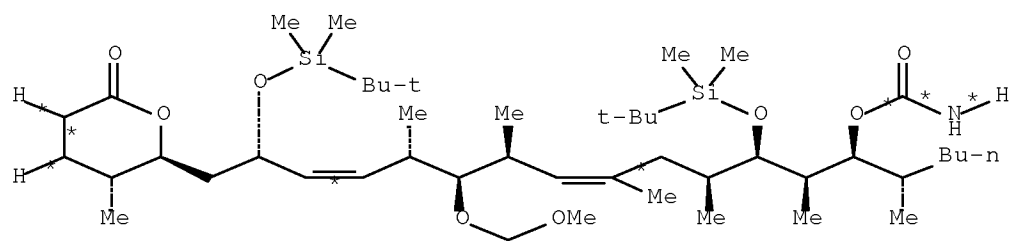


N



AX

6
STEPS
→



U
YIELD 85%

RX(22) RCT BM 837383-29-6
 RGT AU 1333-74-0 H2
 PRO M 870075-20-0
 CAT 12135-22-7 Pd(OH)2
 SOL 141-78-6 AcOEt

RX(3) RCT M 870075-20-0

STAGE(1)
 RGT E 144-55-8 NaHCO3, O 87413-09-0 Martin's reagent
 SOL 75-09-2 CH2Cl2
 CON 2.5 hours, room temperature

STAGE(2)
 RGT P 7772-98-7 Na2S2O3, E 144-55-8 NaHCO3
 SOL 7732-18-5 Water
 CON room temperature

PRO N 853055-22-8

RX(20) RCT B 870074-98-9, BI 852049-56-0
 RGT BK 534-17-8 Cs2CO3
 PRO BJ 870075-18-6
 CAT 72287-26-4 Palladium, [1,1'-bis(diphenylphosphino-
 κP)ferrocene]dichloro-, (SP-4-2)-
 NTE Suzuki coupling

RX(21) RCT BJ 870075-18-6
 RGT W 7647-01-0 HCl
 PRO I 870075-19-7
 SOL 7732-18-5 Water

RX(2) RCT I 870075-19-7

STAGE(1)
 RGT K 7553-56-2 I2, C 603-35-0 PPh3, D 288-32-4 1H-Imidazole

STAGE(2)
 RCT C 603-35-0
 RGT L 121-44-8 Et3N
 CON 100 deg C

PRO J 870074-99-0
 NTE Wittig salt formation in second stage, yield over 4 steps = 65%

RX(23) RCT J 870074-99-0, N 853055-22-8
 RGT AI 917-54-4 MeLi
 PRO R 870075-21-1
 NTE stereoselective, Wittig coupling

RX(4) RCT R 870075-21-1
 RGT T 84-58-2 DDQ
 PRO S 870075-00-6
 NTE yield over 2 steps = 36%

RX(24) RCT S 870075-00-6, AX 3019-71-4
 PRO U 870075-22-2

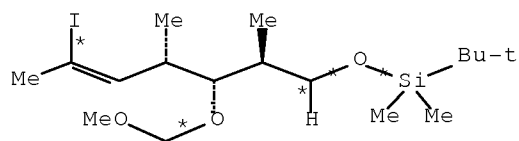
NTE literature preparation

RX(248) OF 268 COMPOSED OF REACTION SEQUENCE RX(27), RX(28), RX(29), RX(30),
RX(31), RX(32), RX(7)

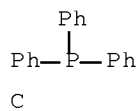
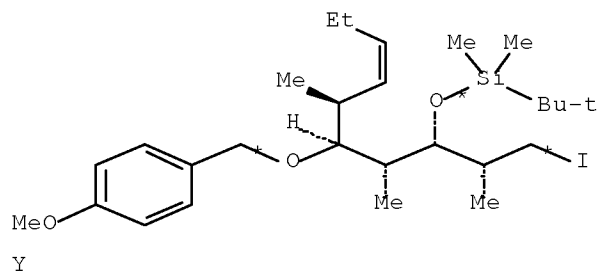
AND REACTION SEQUENCE RX(3), RX(30), RX(31), RX(32), RX(7)

... BI + Y + C ==> BX...

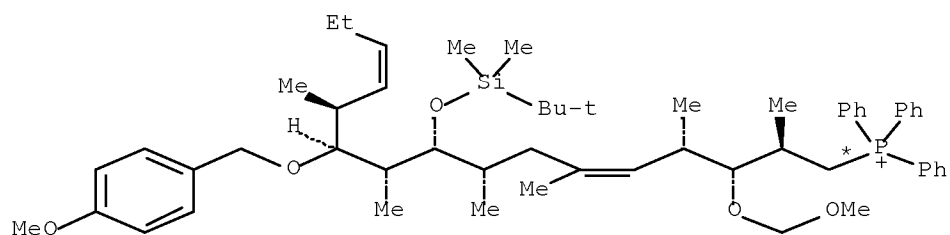
...M + BX + AX ==> AA



BI

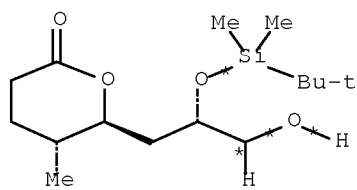


5
STEPS
→

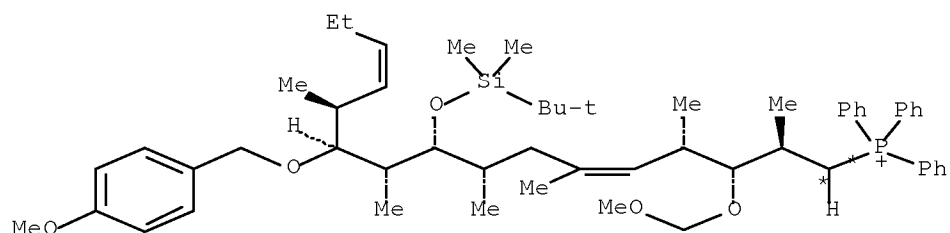


BX

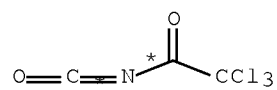
START NEXT REACTION SEQUENCE



M

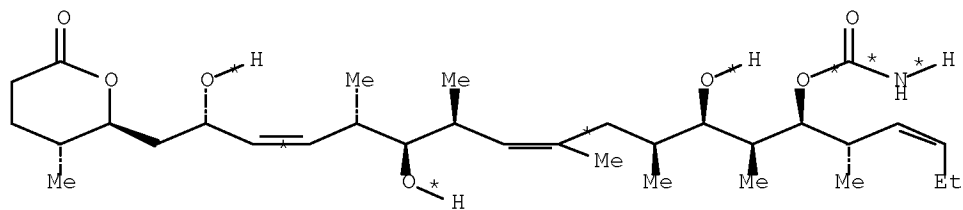


BX



AX

5
STEPS
→



AA
YIELD 70%

RX(27) RCT BI 852049-56-0, Y 870075-02-8
RGT BK 534-17-8 Cs2CO3

PRO BV 870075-26-6
 CAT 72287-26-4 Palladium, [1,1'-bis(diphenylphosphino-
 κP)ferrocene]dichloro-, (SP-4-2)-
 NTE Suzuki coupling

RX(28) RCT BV 870075-26-6
 RGT W 7647-01-0 HCl
 PRO BW 870075-27-7
 SOL 7732-18-5 Water
 NTE regioselective

RX(29) RCT BW 870075-27-7

STAGE(1)
 RGT K 7553-56-2 I2, C 603-35-0 PPh3, D 288-32-4 1H-Imidazole

STAGE(2)
 RCT C 603-35-0
 RGT L 121-44-8 Et3N
 CON 100 deg C

PRO BX 870075-28-8
 NTE stereoselective, Wittig salt formation in second stage

RX(3) RCT M 870075-20-0

STAGE(1)
 RGT E 144-55-8 NaHCO3, O 87413-09-0 Martin's reagent
 SOL 75-09-2 CH2Cl2
 CON 2.5 hours, room temperature

STAGE(2)
 RGT P 7772-98-7 Na2S2O3, E 144-55-8 NaHCO3
 SOL 7732-18-5 Water
 CON room temperature

PRO N 853055-22-8

RX(30) RCT N 853055-22-8, BX 870075-28-8
 RGT AU 1333-74-0 H2
 PRO BY 870075-29-9
 CAT 12135-22-7 Pd(OH)2
 SOL 141-78-6 AcOEt
 NTE Wittig coupling

RX(31) RCT BY 870075-29-9
 RGT T 84-58-2 DDQ
 PRO BZ 870075-30-2

RX(32) RCT BZ 870075-30-2, AX 3019-71-4
 PRO Z 870075-31-3
 NTE literature preparation

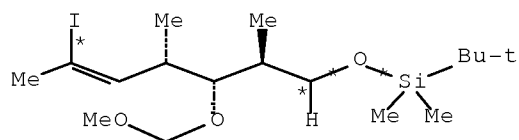
RX(7) RCT Z 870075-31-3
 RGT W 7647-01-0 HCl
 PRO AA 870075-03-9
 SOL 7732-18-5 Water
 NTE yield over 8 steps = 17%

RX(254) OF 268 COMPOSED OF REACTION SEQUENCE RX(27), RX(28), RX(29), RX(30),
RX(31), RX(32)

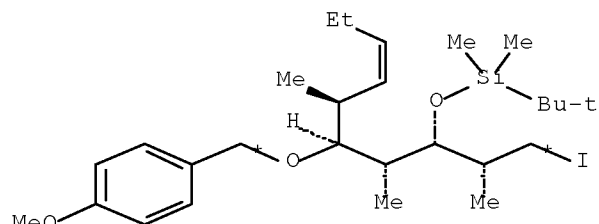
AND REACTION SEQUENCE RX(22), RX(3), RX(30), RX(31), RX(32)

... BI + Y + C ==> BX...

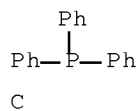
...BM + BX + AX ==> Z



BI

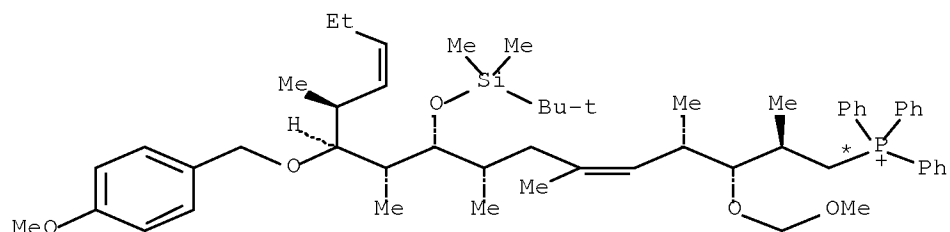


Y



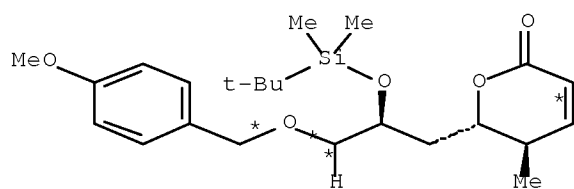
C

5
STEPS
→

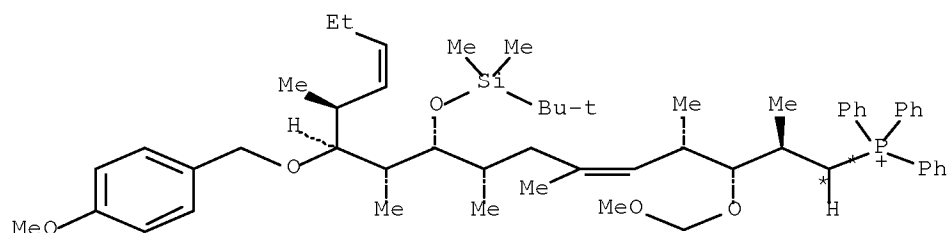


BX

START NEXT REACTION SEQUENCE

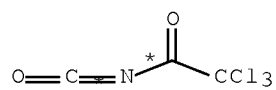


BM



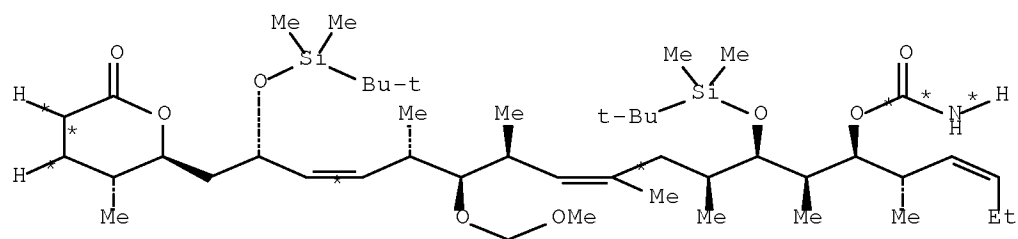
● I⁻

BX



AX

5
STEPS
→



Z
YIELD 79%

RX(27) RCT BI 852049-56-0, Y 870075-02-8

RGT BK 534-17-8 Cs2CO3
 PRO BV 870075-26-6
 CAT 72287-26-4 Palladium, [1,1'-bis(diphenylphosphino-
 κP)ferrocene]dichloro-, (SP-4-2)-
 NTE Suzuki coupling

RX(28) RCT BV 870075-26-6
 RGT W 7647-01-0 HCl
 PRO BW 870075-27-7
 SOL 7732-18-5 Water
 NTE regioselective

RX(29) RCT BW 870075-27-7

STAGE(1)
 RGT K 7553-56-2 I2, C 603-35-0 PPh3, D 288-32-4 1H-Imidazole

STAGE(2)
 RCT C 603-35-0
 RGT L 121-44-8 Et3N
 CON 100 deg C

PRO BX 870075-28-8
 NTE stereoselective, Wittig salt formation in second stage

RX(22) RCT BM 837383-29-6
 RGT AU 1333-74-0 H2
 PRO M 870075-20-0
 CAT 12135-22-7 Pd(OH)2
 SOL 141-78-6 AcOEt

RX(3) RCT M 870075-20-0

STAGE(1)
 RGT E 144-55-8 NaHCO3, O 87413-09-0 Martin's reagent
 SOL 75-09-2 CH2Cl2
 CON 2.5 hours, room temperature

STAGE(2)
 RGT P 7772-98-7 Na2S2O3, E 144-55-8 NaHCO3
 SOL 7732-18-5 Water
 CON room temperature

PRO N 853055-22-8

RX(30) RCT N 853055-22-8, BX 870075-28-8
 RGT AU 1333-74-0 H2
 PRO BY 870075-29-9
 CAT 12135-22-7 Pd(OH)2
 SOL 141-78-6 AcOEt
 NTE Wittig coupling

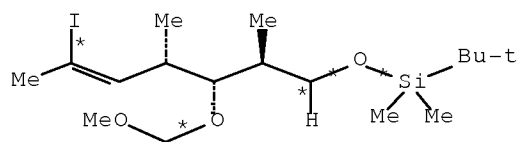
RX(31) RCT BY 870075-29-9
 RGT T 84-58-2 DDQ
 PRO BZ 870075-30-2

RX(32) RCT BZ 870075-30-2, AX 3019-71-4
 PRO Z 870075-31-3
 NTE literature preparation

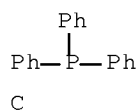
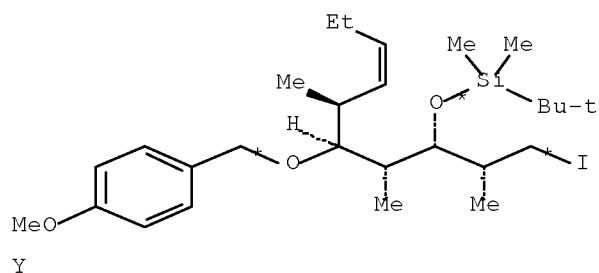
RX(258) OF 268 COMPOSED OF REACTION SEQUENCE RX(27), RX(28), RX(29), RX(30),
 RX(31), RX(32), RX(7)
 AND REACTION SEQUENCE RX(22), RX(3), RX(30), RX(31), RX(32),
 RX(7)

... BI + Y + C ==> BX...

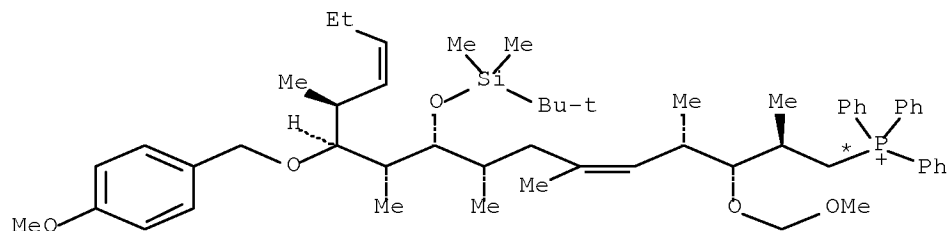
...BM + BX + AX ==> AA



BI

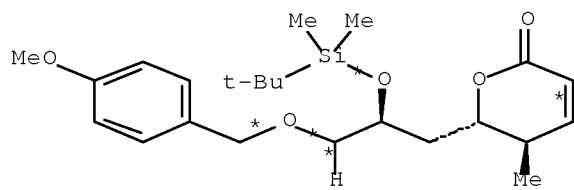


6
STEPS
→

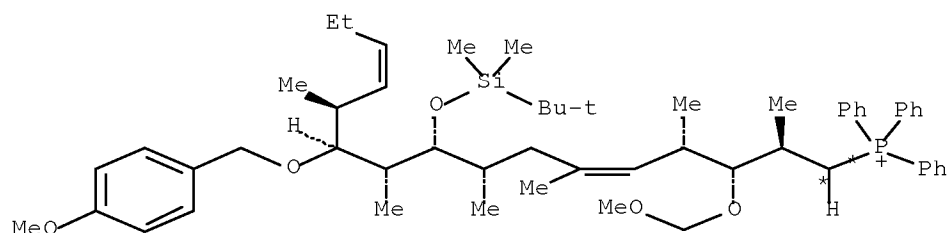


BX

START NEXT REACTION SEQUENCE

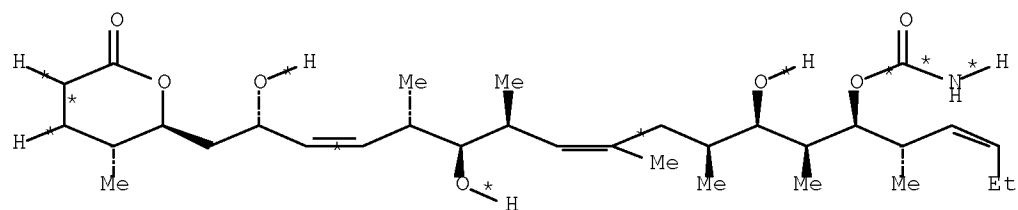
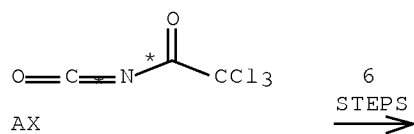


BM



● I⁻

BX



AA
YIELD 70%

RX(27) RCT BI 852049-56-0, Y 870075-02-8
RGT BK 534-17-8 Cs2CO3

PRO BV 870075-26-6
 CAT 72287-26-4 Palladium, [1,1'-bis(diphenylphosphino-
 κP)ferrocene]dichloro-, (SP-4-2)-
 NTE Suzuki coupling

RX(28) RCT BV 870075-26-6
 RGT W 7647-01-0 HCl
 PRO BW 870075-27-7
 SOL 7732-18-5 Water
 NTE regioselective

RX(29) RCT BW 870075-27-7

STAGE(1)
 RGT K 7553-56-2 I2, C 603-35-0 PPh3, D 288-32-4 1H-Imidazole

STAGE(2)
 RCT C 603-35-0
 RGT L 121-44-8 Et3N
 CON 100 deg C

PRO BX 870075-28-8
 NTE stereoselective, Wittig salt formation in second stage

RX(22) RCT BM 837383-29-6
 RGT AU 1333-74-0 H2
 PRO M 870075-20-0
 CAT 12135-22-7 Pd(OH)2
 SOL 141-78-6 AcOEt

RX(3) RCT M 870075-20-0

STAGE(1)
 RGT E 144-55-8 NaHCO3, O 87413-09-0 Martin's reagent
 SOL 75-09-2 CH2Cl2
 CON 2.5 hours, room temperature

STAGE(2)
 RGT P 7772-98-7 Na2S2O3, E 144-55-8 NaHCO3
 SOL 7732-18-5 Water
 CON room temperature

PRO N 853055-22-8

RX(30) RCT N 853055-22-8, BX 870075-28-8
 RGT AU 1333-74-0 H2
 PRO BY 870075-29-9
 CAT 12135-22-7 Pd(OH)2
 SOL 141-78-6 AcOEt
 NTE Wittig coupling

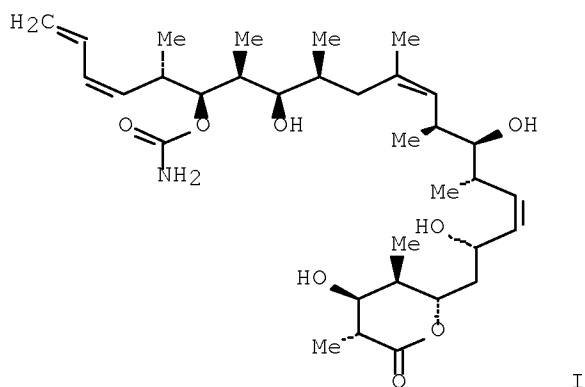
RX(31) RCT BY 870075-29-9
 RGT T 84-58-2 DDQ
 PRO BZ 870075-30-2

RX(32) RCT BZ 870075-30-2, AX 3019-71-4
 PRO Z 870075-31-3
 NTE literature preparation

RX(7) RCT Z 870075-31-3

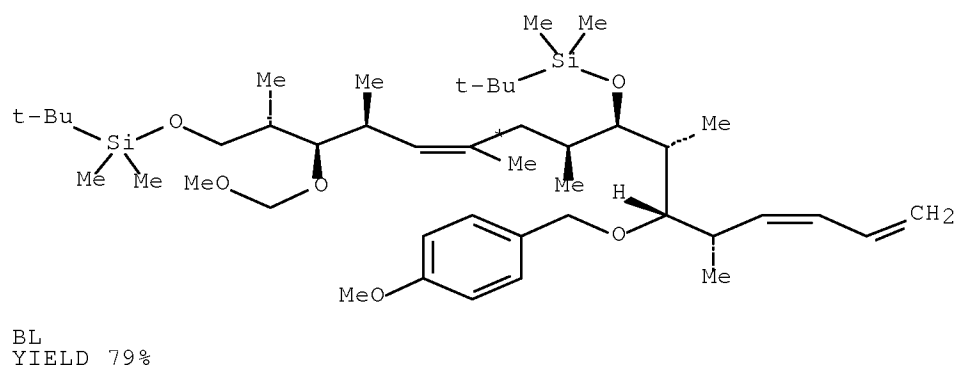
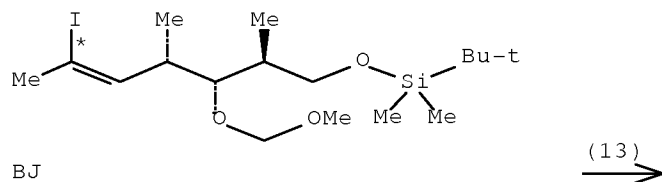
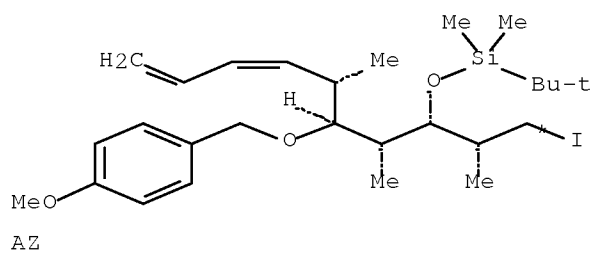
RGT W 7647-01-0 HCl
PRO AA 870075-03-9
SOL 7732-18-5 Water
NTE yield over 8 steps = 17%

L3 ANSWER 5 OF 9 CASREACT COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 142:481865 CASREACT Full-text
TITLE: Total Synthesis of (+)-Discodermolide: A Highly
Convergent Fourth-Generation Approach
AUTHOR(S): Smith, Amos B., III; Freeze, B. Scott; Xian, Ming;
Hirose, Tomoyasu
CORPORATE SOURCE: Department of Chemistry, University of Pennsylvania,
Philadelphia, PA, 19104, USA
SOURCE: Organic Letters (2005), 7(9), 1825-1828
CODEN: ORLEF7; ISSN: 1523-7060
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



AB A highly convergent, fourth-generation total synthesis of (+)-discodermolide (I), with a longest linear sequence of 17 steps and an overall yield of 9.0%, has been achieved. Highlighting the strategy is the efficient construction and sequential, bidirectional union of a linchpin comprising the C(9)-C(14) Wittig salt-vinyl iodide (-)-18. Importantly, Wittig salt generation proceeded in excellent yield under ambient pressure.
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(13) OF 178 ...AZ + BJ ==> BL



RX(13) RCT AZ 850211-69-7

STAGE(1)

RGT BM 750545-03-0 Borate(1-),
1,5-cyclooctanediylhydromethoxy-, (T-4)-, AS 594-19-4
t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> room temperature
SUBSTAGE(3) 1 hour, room temperature

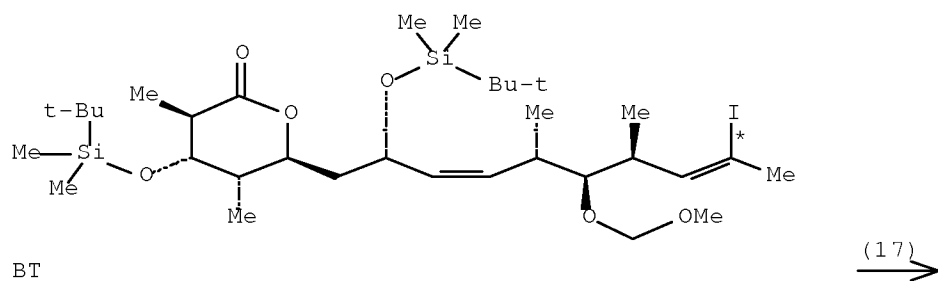
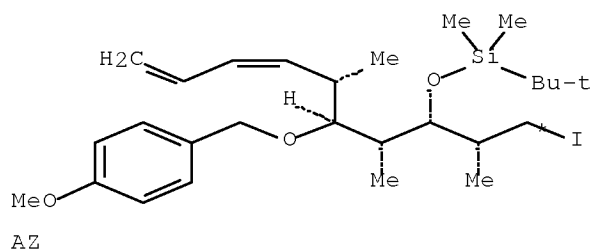
STAGE(2)

RCT BJ 852049-56-0
RGT BN 534-17-8 Cs2CO3
CAT 72287-26-4 Palladium,

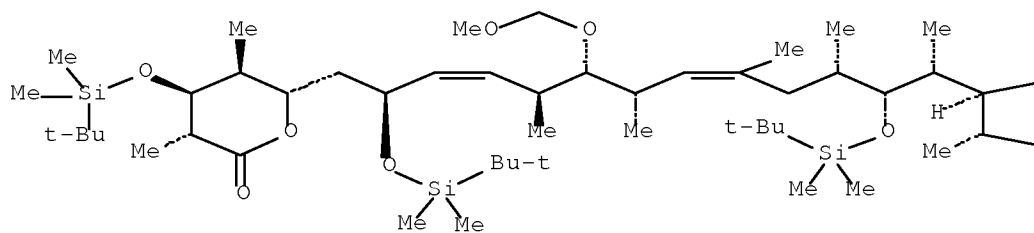
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

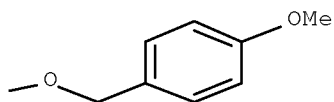
PRO BL 633293-91-1
 NTE in the dark

RX(17) OF 178 ...AZ + BT ==> EV



PAGE 1-A





BV
YIELD 40%

RX(17) RCT AZ 850211-69-7

STAGE(1)

RGT BM 750545-03-0 Borate(1-),
1,5-cyclooctanediylhydromethoxy-, (T-4)-, AS 594-19-4
t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> room temperature
SUBSTAGE(3) 1 hour, room temperature

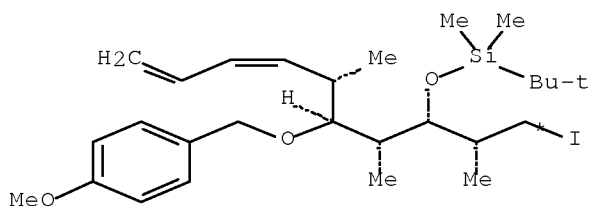
STAGE(2)

RCT BT 850211-74-4
RGT BW 603-32-7 Ph3As, BN 534-17-8 Cs2CO3
CAT 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water
CON 20 hours, room temperature

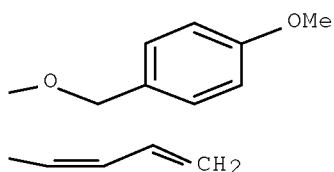
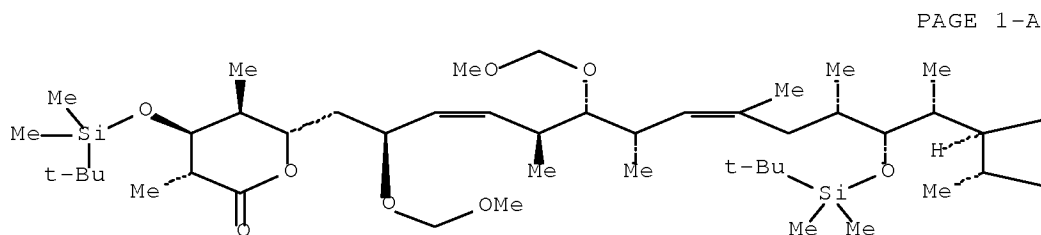
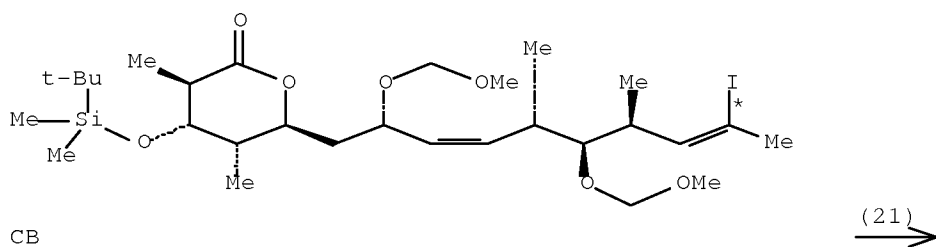
PRO BV 633293-75-1

NTE in the dark

RX(21) OF 178 ...AZ + CB ==> CC...



AZ



PAGE 1-B

RX(21) RCT AZ 850211-69-7

STAGE(1)

RGT BM 750545-03-0 Borate(1-),
 1,5-cyclooctanediylhydromethoxy-, (T-4)-, AS 594-19-4
 t-BuLi
 SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
 Pentane
 CON SUBSTAGE(1) -78 deg C
 SUBSTAGE(2) -78 deg C -> room temperature
 SUBSTAGE(3) 1 hour, room temperature

STAGE(2)

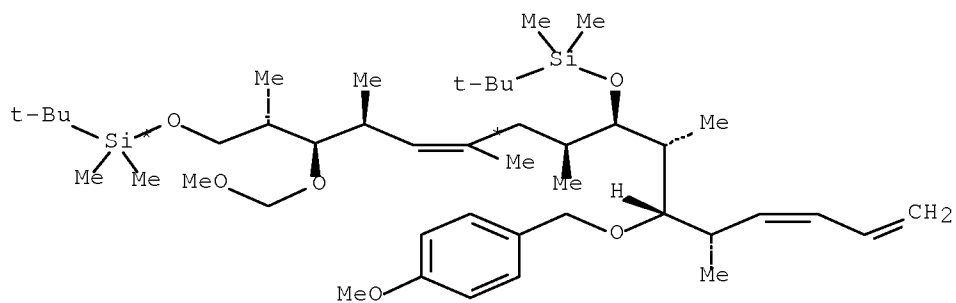
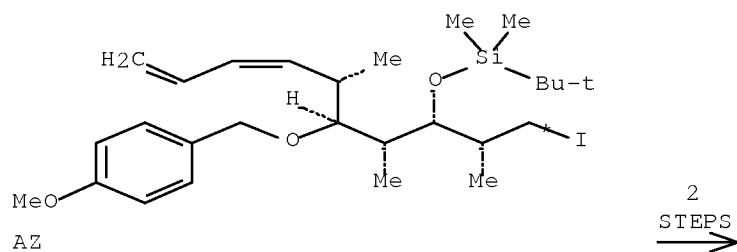
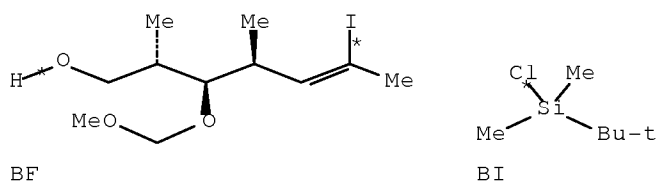
RCT CB 852049-58-2
 RGT BW 603-32-7 Ph3As, BN 534-17-8 Cs2CO3
 CAT 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,

(SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

PRO CC 852049-59-3

RX(39) OF 178 COMPOSED OF RX(12), RX(13)

RX(39) BF + BI + AZ ==> BL



YIELD 79%

RX(12) RCT BF 850211-70-0, BI 18162-48-6

STAGE(1)

RGT BC 288-32-4 1H-Imidazole

SOL 75-09-2 CH2Cl2
CON 15 hours, room temperature

STAGE(2)

RGT BK 7647-14-5 NaCl
SOL 7732-18-5 Water
CON room temperature

PRO BJ 852049-56-0

RX(13) RCT AZ 850211-69-7

STAGE(1)

RGT BM 750545-03-0 Borate(1-),
1,5-cyclooctanediylhydromethoxy-, (T-4)-, AS 594-19-4
t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> room temperature
SUBSTAGE(3) 1 hour, room temperature

STAGE(2)

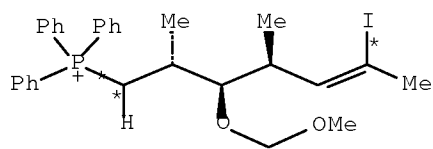
RCT BJ 852049-56-0
RGT BN 534-17-8 Cs2CO3
CAT 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

PRO BL 633293-91-1

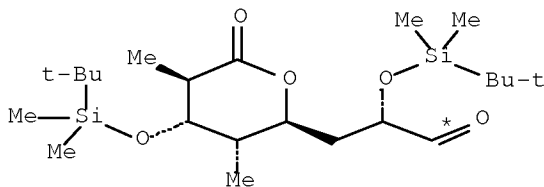
NTE in the dark

RX(43) OF 178 COMPOSED OF RX(16), RX(17)

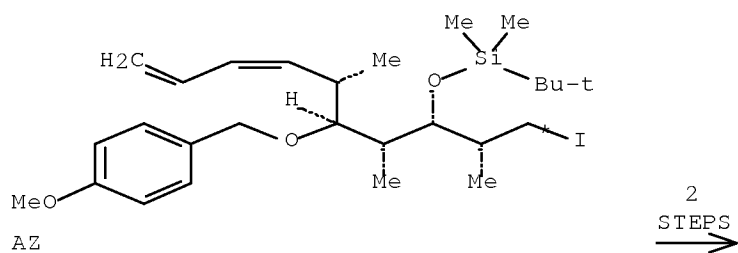
RX(43) BR + BS + AZ ==> BV



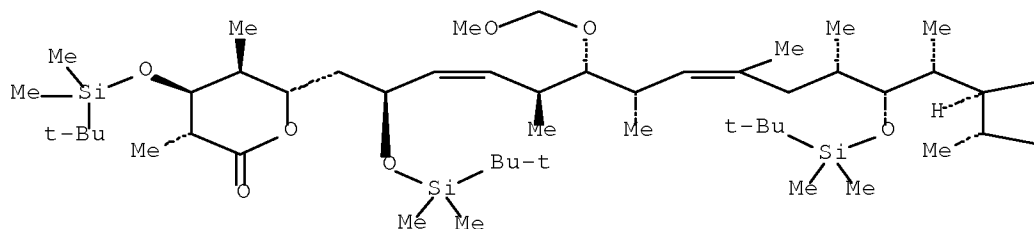
BR



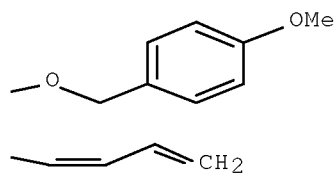
BS



PAGE 1-A



PAGE 1-B



BV
YIELD 40%

RX(16) RCT BR 850211-72-2

STAGE(1)

RGT BU 1070-89-9 (Me₃Si)₂N.Na
SOL 109-99-9 THF
CON 1 hour, -78 deg C

STAGE(2)

RCT BS 252342-51-1
SOL 109-99-9 THF
CON SUBSTAGE(1) 2 hours, -78 deg C
SUBSTAGE(2) -78 deg C -> -10 deg C
SUBSTAGE(3) 2 hours, -10 deg C

STAGE(3)

RGT AJ 12125-02-9 NH₄Cl

SOL 7732-18-5 Water, 60-29-7 Et2O

PRO BT 850211-74-4

RX(17) RCT AZ 850211-69-7

STAGE(1)

RGT BM 750545-03-0 Borate(1-),
1,5-cyclooctanediylhydromethoxy-, (T-4)-, AS 594-19-4
t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> room temperature
SUBSTAGE(3) 1 hour, room temperature

STAGE(2)

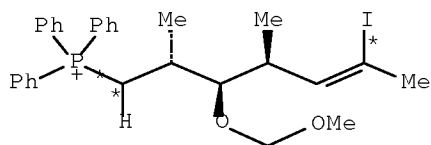
RCT BT 850211-74-4
RGT BW 603-32-7 Ph3As, BN 534-17-8 Cs2CO3
CAT 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water
CON 20 hours, room temperature

PRO BV 633293-75-1

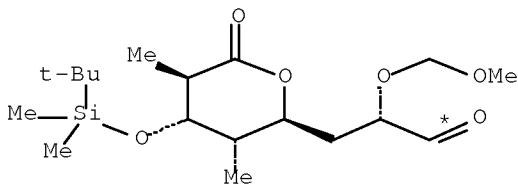
NTE in the dark

RX(46) OF 178 COMPOSED OF RX(20), RX(21)

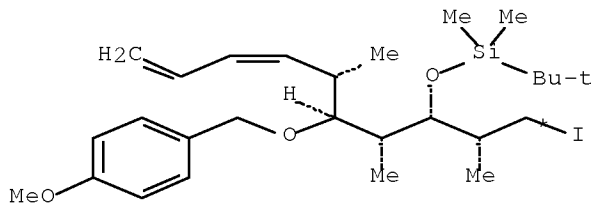
RX(46) BF + CA + AZ ==> CC



BR



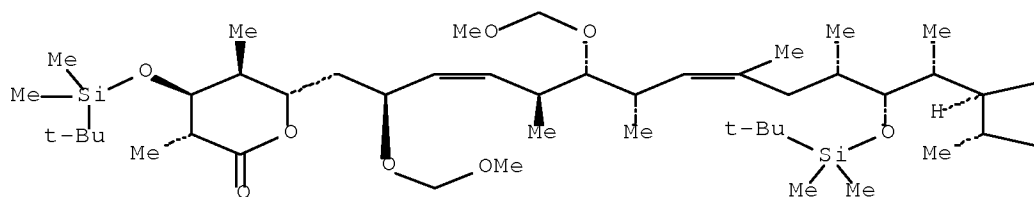
CA



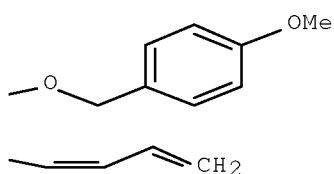
AZ

2
STEPS
→

PAGE 1-A



PAGE 1-B



CC
YIELD 60%

RX(20) RCT BR 850211-72-2

STAGE(1)

RGT BU 1070-89-9 (Me₃Si)₂N.Na

SOL 109-99-9 THF

CON 1 hour, -78 deg C

STAGE(2)

RCT CA 852049-57-1

SOL 109-99-9 THF

CON SUBSTAGE(1) 2 hours, -78 deg C

SUBSTAGE(2) -78 deg C -> -10 deg C

SUBSTAGE(3) 2 hours, -10 deg C

STAGE(3)

RGT AJ 12125-02-9 NH₄Cl

SOL 7732-18-5 Water, 60-29-7 Et₂O

PRO CB 852049-58-2

RX(21) RCT AZ 850211-69-7

STAGE(1)

RGT BM 750545-03-0 Borate(1-),
1,5-cyclooctanediylhydromethoxy-, (T-4)-, AS 594-19-4
t-BuLi

SOL 60-29-7 Et₂O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane

CON SUBSTAGE(1) -78 deg C

SUBSTAGE(2) -78 deg C -> room temperature

SUBSTAGE(3) 1 hour, room temperature

STAGE(2)

RCT CB 852049-58-2

RGT BW 603-32-7 Ph3As, BN 534-17-8 Cs2CO3

CAT 72287-26-4 Palladium,

[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-

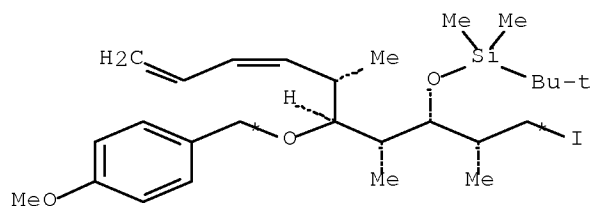
SOL 7732-18-5 Water, 68-12-2 DMF

CON 20 hours, room temperature

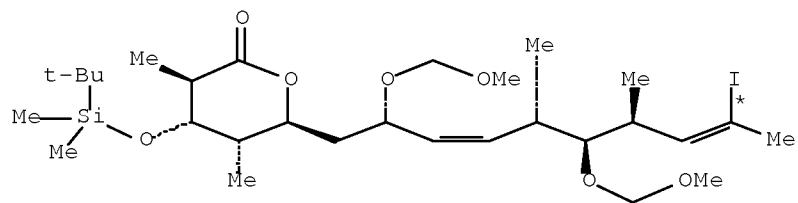
PRO CC 852049-59-3

RX(47) OF 178 COMPOSED OF RX(21), RX(22)

RX(47) AZ + CB ==> CD



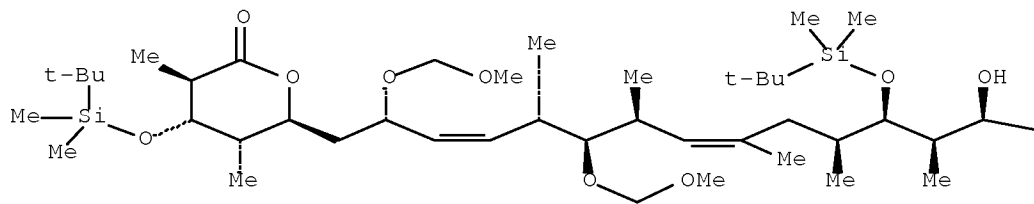
AZ

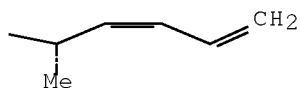


CB

2
STEPS
→

PAGE 1-A





CD
YIELD 91%

RX(21) RCT AZ 850211-69-7

STAGE(1)

RGT BM 750545-03-0 Borate(1-),
1,5-cyclooctanediylhydromethoxy-, (T-4)-, AS 594-19-4
t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> room temperature
SUBSTAGE(3) 1 hour, room temperature

STAGE(2)

RCT CB 852049-58-2
RGT BW 603-32-7 Ph3As, BN 534-17-8 Cs2CO3
CAT 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

PRO CC 852049-59-3

RX(22) RCT CC 852049-59-3

STAGE(1)

RGT BG 84-58-2 DDQ
SOL 7732-18-5 Water, 75-09-2 CH2Cl2
CON SUBSTAGE(1) 30 minutes, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature
SUBSTAGE(3) 15 minutes, room temperature

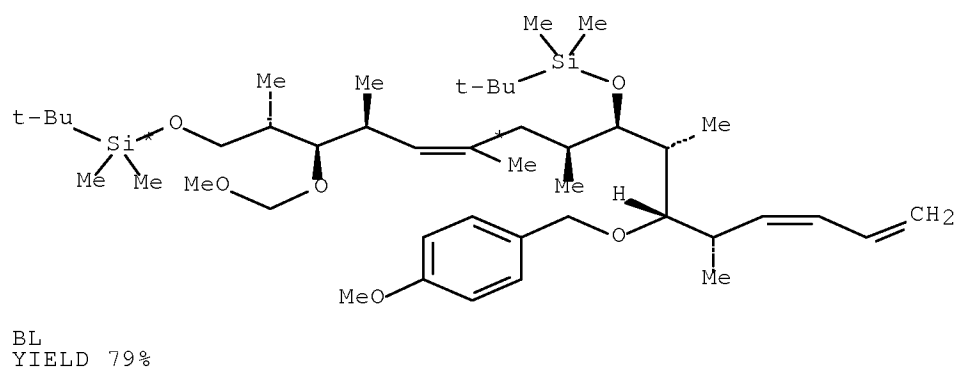
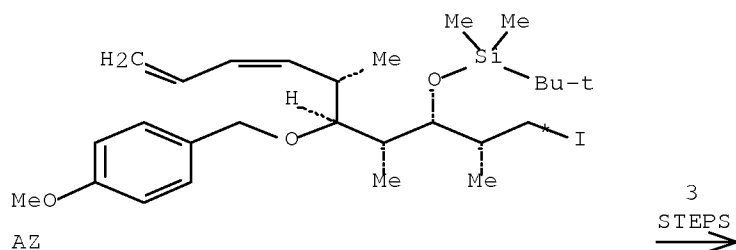
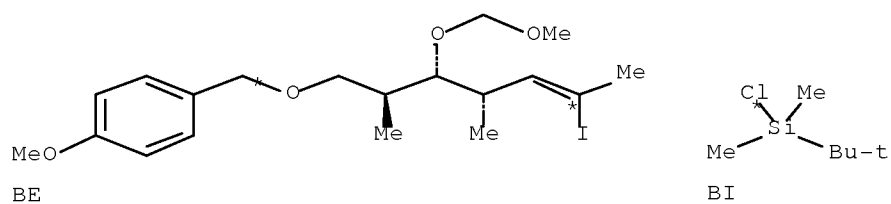
STAGE(2)

RGT BH 144-55-8 NaHCO3
SOL 7732-18-5 Water
CON room temperature

PRO CD 852049-60-6

RX(73) OF 178 COMPOSED OF RX(11), RX(12), RX(13)

RX(73) BE + BI + AZ ==> BL



RX(11) RCT BE 633294-02-7

STAGE(1)

RGT BG 84-58-2 DDQ
 SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
 CON 2 hours, 0 deg C

STAGE(2)

RGT BH 144-55-8 NaHCO₃
 SOL 7732-18-5 Water

PRO BF 850211-70-0

RX(12) RCT BF 850211-70-0, BI 18162-48-6

STAGE(1)
 RGT BC 288-32-4 1H-Imidazole
 SOL 75-09-2 CH2Cl2
 CON 15 hours, room temperature

STAGE(2)
 RGT BK 7647-14-5 NaCl
 SOL 7732-18-5 Water
 CON room temperature

PRO BJ 852049-56-0

RX(13) RCT AZ 850211-69-7

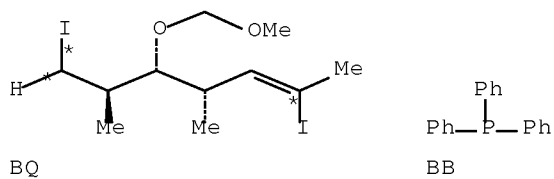
STAGE(1)
 RGT BM 750545-03-0 Borate(1-),
 1,5-cyclooctanediylhydromethoxy-, (T-4)-, AS 594-19-4
 t-BuLi
 SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
 Pentane
 CON SUBSTAGE(1) -78 deg C
 SUBSTAGE(2) -78 deg C -> room temperature
 SUBSTAGE(3) 1 hour, room temperature

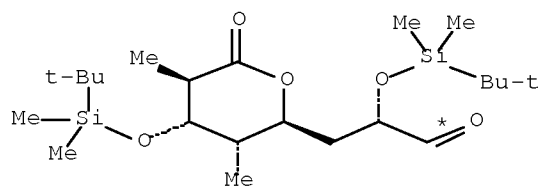
STAGE(2)
 RCT BJ 852049-56-0
 RGT BN 534-17-8 Cs2CO3
 CAT 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

PRO BL 633293-91-1
 NTE in the dark

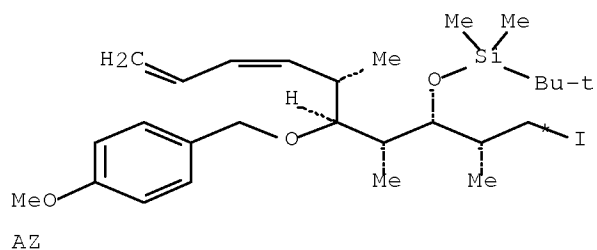
RX(79) OF 178 COMPOSED OF RX(15), RX(16), RX(17)

RX(79) BQ + BB + BS + AZ ==> BV



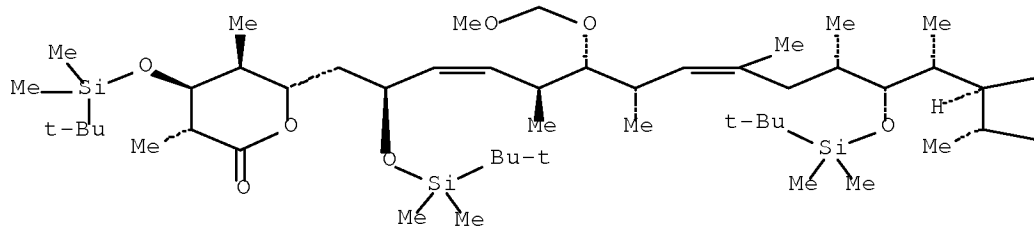


BS

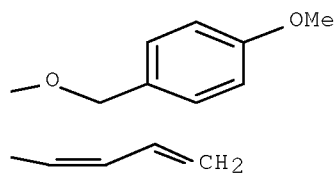


3
STEPS
→

PAGE 1-A



PAGE 1-B



BV
YIELD 40%

RX(15) RCT BQ 850211-71-1, BB 603-35-0
PRO BR 850211-72-2
CON SUBSTAGE(1) room temperature -> 95 deg C

SUBSTAGE(2) 18 hours, 95 deg C

RX(16) RCT BR 850211-72-2

STAGE(1)

RGT BU 1070-89-9 (Me3Si)2N.Na

SOL 109-99-9 THF

CON 1 hour, -78 deg C

STAGE(2)

RCT BS 252342-51-1

SOL 109-99-9 THF

CON SUBSTAGE(1) 2 hours, -78 deg C

SUBSTAGE(2) -78 deg C -> -10 deg C

SUBSTAGE(3) 2 hours, -10 deg C

STAGE(3)

RGT AJ 12125-02-9 NH4Cl

SOL 7732-18-5 Water, 60-29-7 Et2O

PRO BT 850211-74-4

RX(17) RCT AZ 850211-69-7

STAGE(1)

RGT BM 750545-03-0 Borate(1-),

1,5-cyclooctanediylhydromethoxy-, (T-4)-, AS 594-19-4
t-BuLi

SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane

CON SUBSTAGE(1) -78 deg C

SUBSTAGE(2) -78 deg C -> room temperature

SUBSTAGE(3) 1 hour, room temperature

STAGE(2)

RCT BT 850211-74-4

RGT BW 603-32-7 Ph3As, BN 534-17-8 Cs2CO3

CAT 72287-26-4 Palladium,

[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-

SOL 7732-18-5 Water

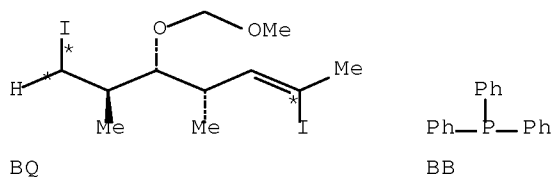
CON 20 hours, room temperature

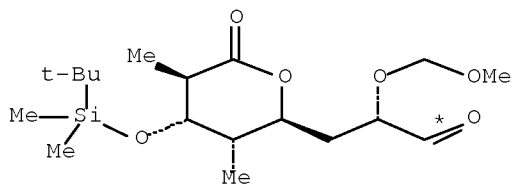
PRO BV 633293-75-1

NTE in the dark

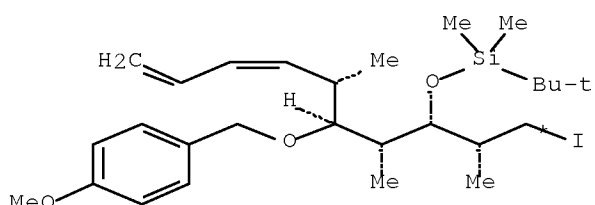
RX(80) OF 178 COMPOSED OF RX(15), RX(20), RX(21)

RX(80) BQ + BB + CA + AZ ==> CC





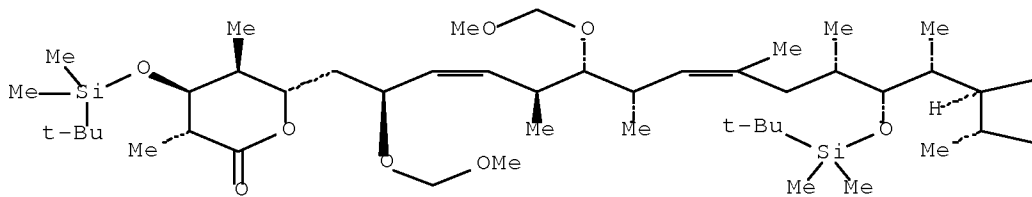
CA



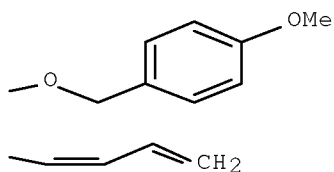
AZ

3
STEPS
→

PAGE 1-A



PAGE 1-B



CC
YIELD 60%

PRO BR 850211-72-2
CON SUBSTAGE(1) room temperature -> 95 deg C
SUBSTAGE(2) 18 hours, 95 deg C

RX(20) RCT BR 850211-72-2

STAGE(1)
RGT BU 1070-89-9 (Me3Si)2N.Na
SOL 109-99-9 THF
CON 1 hour, -78 deg C

STAGE(2)
RCT CA 852049-57-1
SOL 109-99-9 THF
CON SUBSTAGE(1) 2 hours, -78 deg C
SUBSTAGE(2) -78 deg C -> -10 deg C
SUBSTAGE(3) 2 hours, -10 deg C

STAGE(3)
RGT AJ 12125-02-9 NH4Cl
SOL 7732-18-5 Water, 60-29-7 Et2O

PRO CB 852049-58-2

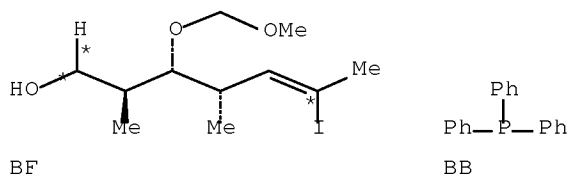
RX(21) RCT AZ 850211-69-7

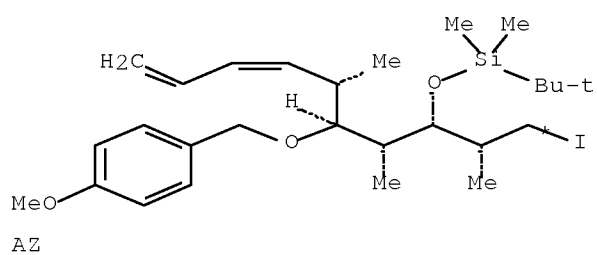
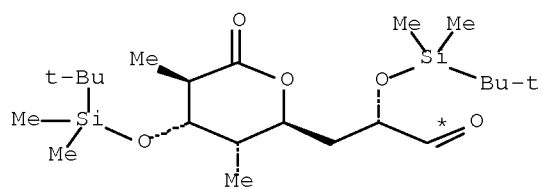
STAGE(1)
RGT BM 750545-03-0 Borate(1-),
1,5-cyclooctanediylhydromethoxy-, (T-4)-, AS 594-19-4
t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> room temperature
SUBSTAGE(3) 1 hour, room temperature

STAGE(2)
RCT CB 852049-58-2
RGT BW 603-32-7 Ph3As, BN 534-17-8 Cs2CO3
CAT 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

PRO CC 852049-59-3

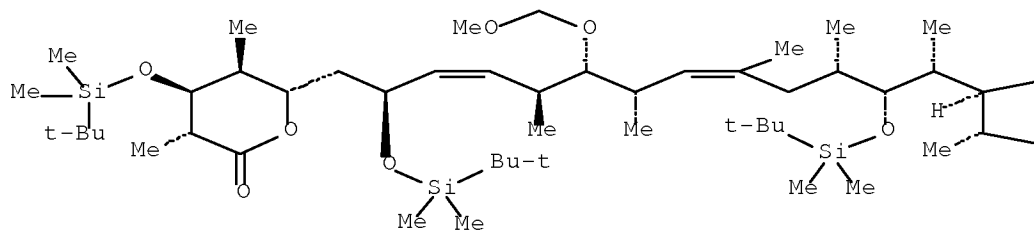
RX(81) OF 178 COMPOSED OF RX(14), RX(15), RX(16), RX(17)
RX(81) BF + BB + BS + AZ ==> BV



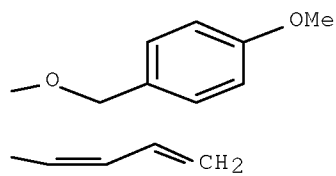


4
STEPS
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PAGE 1-A



PAGE 1-B



BV
YIELD 40%

RX(14) RCT BF 850211-70-0

STAGE(1)
 RGT BA 7553-56-2 I2, BB 603-35-0 PPh3, BC 288-32-4 1H-Imidazole
 SOL 60-29-7 Et2O, 71-43-2 Benzene
 CON SUBSTAGE(1) 0 deg C -> room temperature
 SUBSTAGE(2) 12 hours, room temperature

STAGE(2)
 RGT BH 144-55-8 NaHCO3
 SOL 7732-18-5 Water
 CON room temperature

PRO BQ 850211-71-1

RX(15) RCT BQ 850211-71-1, BB 603-35-0
 PRO BR 850211-72-2
 CON SUBSTAGE(1) room temperature -> 95 deg C
 SUBSTAGE(2) 18 hours, 95 deg C

RX(16) RCT BR 850211-72-2

STAGE(1)
 RGT BU 1070-89-9 (Me3Si)2N.Na
 SOL 109-99-9 THF
 CON 1 hour, -78 deg C

STAGE(2)
 RCT BS 252342-51-1
 SOL 109-99-9 THF
 CON SUBSTAGE(1) 2 hours, -78 deg C
 SUBSTAGE(2) -78 deg C -> -10 deg C
 SUBSTAGE(3) 2 hours, -10 deg C

STAGE(3)
 RGT AJ 12125-02-9 NH4Cl
 SOL 7732-18-5 Water, 60-29-7 Et2O

PRO BT 850211-74-4

RX(17) RCT AZ 850211-69-7

STAGE(1)
 RGT BM 750545-03-0 Borate(1-),
 1,5-cyclooctanediylhydromethoxy-, (T-4)-, AS 594-19-4
 t-BuLi
 SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
 Pentane
 CON SUBSTAGE(1) -78 deg C
 SUBSTAGE(2) -78 deg C -> room temperature
 SUBSTAGE(3) 1 hour, room temperature

STAGE(2)
 RCT BT 850211-74-4
 RGT BW 603-32-7 Ph3As, BN 534-17-8 Cs2CO3
 CAT 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water

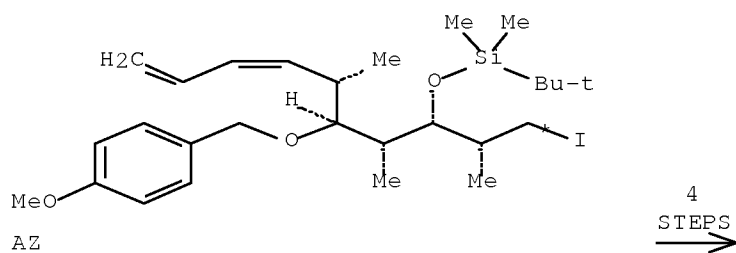
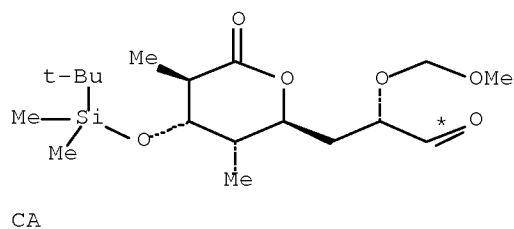
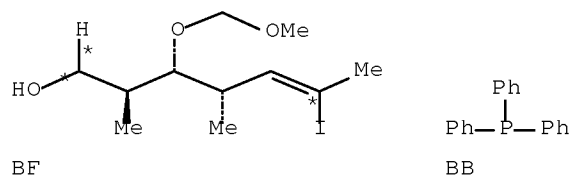
CON 20 hours, room temperature

PRO BV 633293-75-1

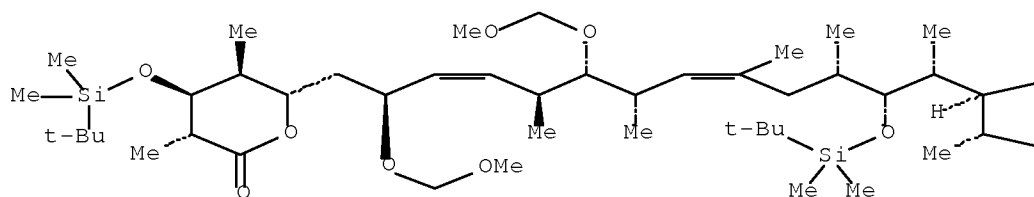
NTE in the dark

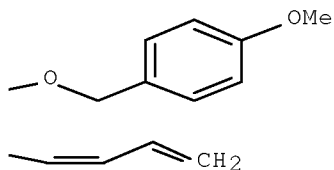
RX(82) OF 178 COMPOSED OF RX(14), RX(15), RX(20), RX(21)

RX(82) BF + BB + CA + AZ ==> CC



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CC
YIELD 60%

RX(14) RCT BF 850211-70-0

STAGE(1)

RGT BA 7553-56-2 I2, BB 603-35-0 PPh3, BC 288-32-4 1H-Imidazole
SOL 60-29-7 Et2O, 71-43-2 Benzene
CON SUBSTAGE(1) 0 deg C -> room temperature
SUBSTAGE(2) 12 hours, room temperature

STAGE(2)

RGT BH 144-55-8 NaHCO3
SOL 7732-18-5 Water
CON room temperature

PRO BQ 850211-71-1

RX(15) RCT BQ 850211-71-1, BB 603-35-0
PRO BR 850211-72-2
CON SUBSTAGE(1) room temperature -> 95 deg C
SUBSTAGE(2) 18 hours, 95 deg C

RX(20) RCT BR 850211-72-2

STAGE(1)

RGT BU 1070-89-9 (Me3Si)2N.Na
SOL 109-99-9 THF
CON 1 hour, -78 deg C

STAGE(2)

RCT CA 852049-57-1
SOL 109-99-9 THF
CON SUBSTAGE(1) 2 hours, -78 deg C
SUBSTAGE(2) -78 deg C -> -10 deg C
SUBSTAGE(3) 2 hours, -10 deg C

STAGE(3)

RGT AJ 12125-02-9 NH4Cl
SOL 7732-18-5 Water, 60-29-7 Et2O

PRO CB 852049-58-2

RX(21) RCT AZ 850211-69-7

STAGE(1)

RGT BM 750545-03-0 Borate(1-),
 1,5-cyclooctanediylhydromethoxy-, (T-4)-, AS 594-19-4
 t-BuLi
 SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
 Pentane
 CON SUBSTAGE(1) -78 deg C
 SUBSTAGE(2) -78 deg C -> room temperature
 SUBSTAGE(3) 1 hour, room temperature

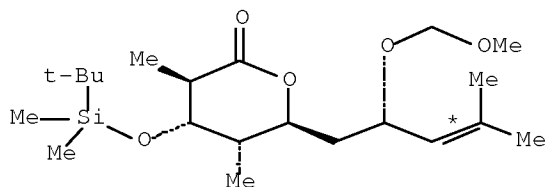
STAGE(2)

RCT CB 852049-58-2
 RGT BW 603-32-7 Ph3As, BN 534-17-8 Cs2CO3
 CAT 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

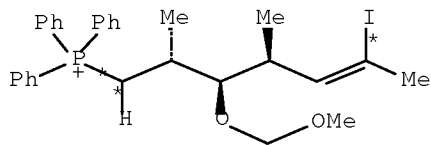
PRO CC 852049-59-3

RX(84) OF 178 COMPOSED OF RX(19), RX(20), RX(21)

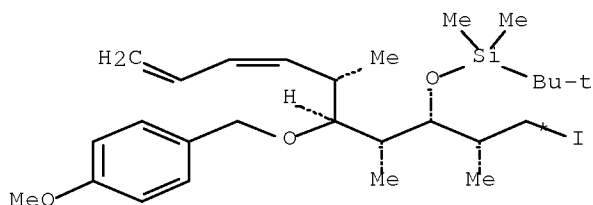
RX(84) BZ + BR + AZ ==> CC



BZ

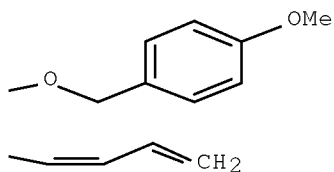
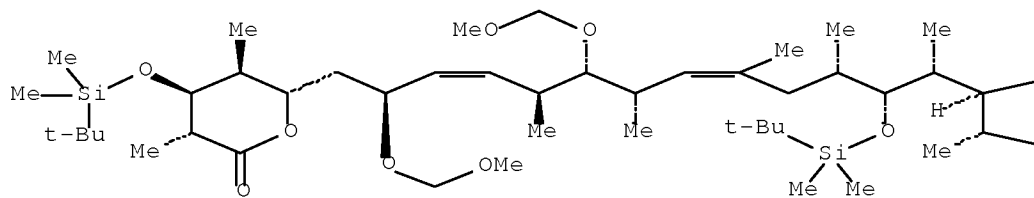


BR



AZ

3
 STEPS
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CC
YIELD 60%

RX(19) RCT BZ 852049-62-8

STAGE(1)

RGT AM 7782-44-7 O2, AN 10028-15-6 Ozone
SOL 75-09-2 CH2Cl2
CON -78 deg C

STAGE(2)

RGT BB 603-35-0 PPh3
CON 1 hour, room temperature

PRO CA 852049-57-1

RX(20) RCT BR 850211-72-2

STAGE(1)

RGT BU 1070-89-9 (Me3Si)2N.Na
SOL 109-99-9 THF
CON 1 hour, -78 deg C

STAGE(2)

RCT CA 852049-57-1
SOL 109-99-9 THF
CON SUBSTAGE(1) 2 hours, -78 deg C
SUBSTAGE(2) -78 deg C -> -10 deg C
SUBSTAGE(3) 2 hours, -10 deg C

STAGE(3)

RGT AJ 12125-02-9 NH4Cl
SOL 7732-18-5 Water, 60-29-7 Et2O

PRO CB 852049-58-2

RX(21) RCT AZ 850211-69-7

STAGE(1)

RGT BM 750545-03-0 Borate(1-),
1,5-cyclooctanediylhydromethoxy-, (T-4)-, AS 594-19-4
t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> room temperature
SUBSTAGE(3) 1 hour, room temperature

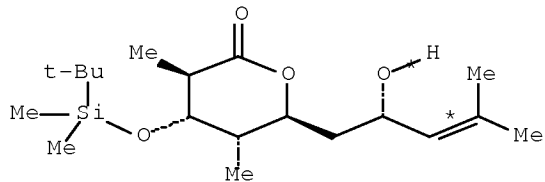
STAGE(2)

RCT CB 852049-58-2
RGT BW 603-32-7 Ph3As, BN 534-17-8 Cs2CO3
CAT 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

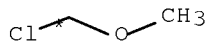
PRO CC 852049-59-3

RX(85) OF 178 COMPOSED OF RX(18), RX(19), RX(20), RX(21)

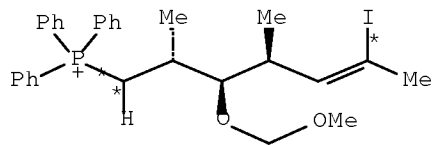
RX(85) BX + BY + ER + AZ ==> CC



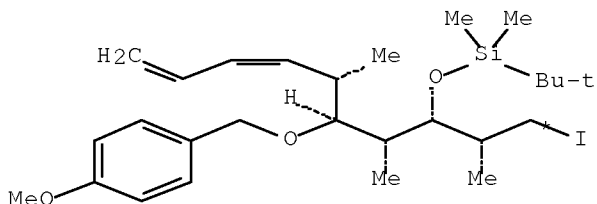
BX



BY



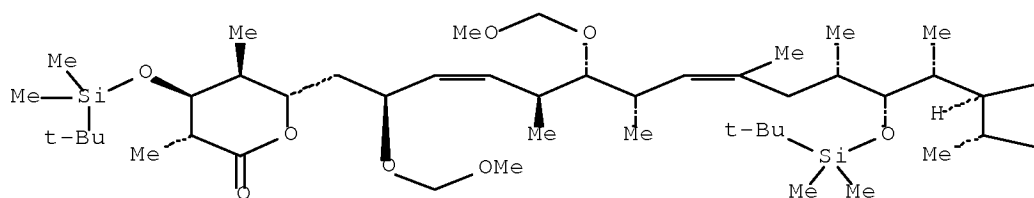
BR



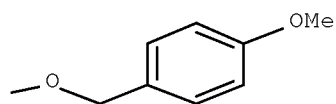
AZ

4
STEPS
→

PAGE 1-A



PAGE 1-B



CC
YIELD 60%

RX(18) RCT BX 256920-77-1, BY 107-30-2

STAGE(1)

RGT H 7087-68-5 EtN(Pr-i)2

SOL 75-09-2 CH2Cl2

CON 12 hours, room temperature

STAGE(2)

RGT BK 7647-14-5 NaCl

SOL 7732-18-5 Water

CON room temperature

PRO BZ 852049-62-8

RX(19) RCT BZ 852049-62-8

STAGE(1)

RGT AM 7782-44-7 O2, AN 10028-15-6 Ozone

SOL 75-09-2 CH2Cl2

CON -78 deg C

STAGE(2)

RGT BB 603-35-0 PPh3

```

        CON  1 hour, room temperature

PRO   CA 852049-57-1

RX(20)  RCT  BR 850211-72-2

        STAGE(1)
        RGT  BU 1070-89-9 (Me3Si)2N.Na
        SOL  109-99-9 THF
        CON  1 hour, -78 deg C

        STAGE(2)
        RCT  CA 852049-57-1
        SOL  109-99-9 THF
        CON  SUBSTAGE(1) 2 hours, -78 deg C
            SUBSTAGE(2) -78 deg C -> -10 deg C
            SUBSTAGE(3) 2 hours, -10 deg C

        STAGE(3)
        RGT  AJ 12125-02-9 NH4Cl
        SOL  7732-18-5 Water, 60-29-7 Et2O

PRO   CB 852049-58-2

RX(21)  RCT  AZ 850211-69-7

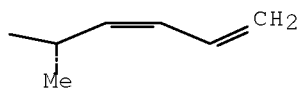
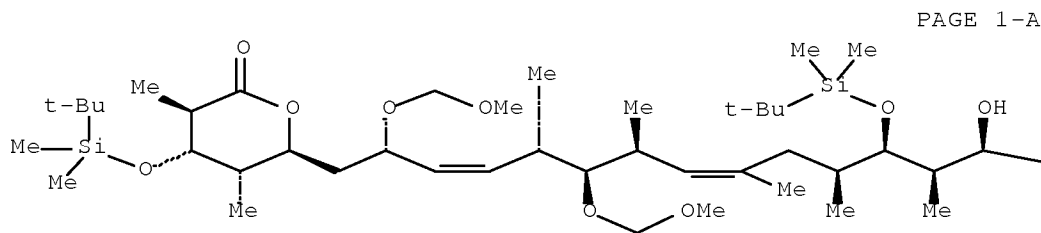
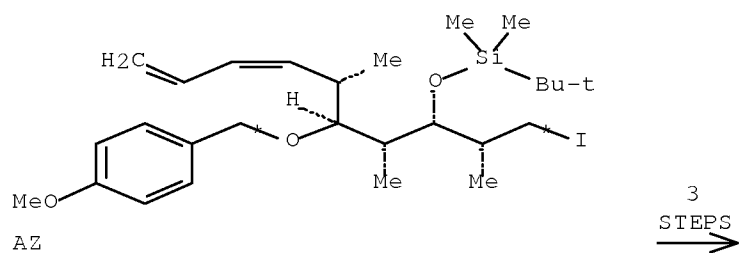
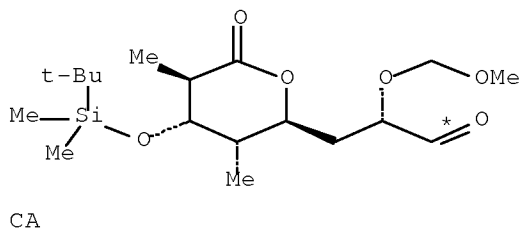
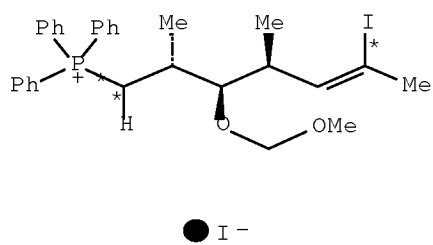
        STAGE(1)
        RGT  BM 750545-03-0 Borate(1-),
            1,5-cyclooctanediylhydromethoxy-, (T-4)-, AS 594-19-4
            t-BuLi
        SOL  60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
            Pentane
        CON  SUBSTAGE(1) -78 deg C
            SUBSTAGE(2) -78 deg C -> room temperature
            SUBSTAGE(3) 1 hour, room temperature

        STAGE(2)
        RCT  CB 852049-58-2
        RGT  BW 603-32-7 Ph3As, BN 534-17-8 Cs2CO3
        CAT  72287-26-4 Palladium,
            [1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
            (SP-4-2)-
        SOL  7732-18-5 Water, 68-12-2 DMF
        CON  20 hours, room temperature

PRO   CC 852049-59-3

RX(86) OF 178 COMPOSED OF RX(20), RX(21), RX(22)
RX(86)  BF + CA + AZ ==> CD

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YIELD 91%

RCT BR 850211-72-2

PAGE 1-A

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STAGE(1)
RGT BU 1070-89-9 (Me3Si)2N.Na
SOL 109-99-9 THF
CON 1 hour, -78 deg C

STAGE(2)
RCT CA 852049-57-1
SOL 109-99-9 THF
CON SUBSTAGE(1) 2 hours, -78 deg C
SUBSTAGE(2) -78 deg C -> -10 deg C
SUBSTAGE(3) 2 hours, -10 deg C

STAGE(3)
RGT AJ 12125-02-9 NH4Cl
SOL 7732-18-5 Water, 60-29-7 Et2O

PRO CB 852049-58-2

RX(21) RCT AZ 850211-69-7

STAGE(1)
RGT BM 750545-03-0 Borate(1-),
1,5-cyclooctanediyldromethoxy-, (T-4)-, AS 594-19-4
t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> room temperature
SUBSTAGE(3) 1 hour, room temperature

STAGE(2)
RCT CB 852049-58-2
RGT BW 603-32-7 Ph3As, BN 534-17-8 Cs2CO3
CAT 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

PRO CC 852049-59-3

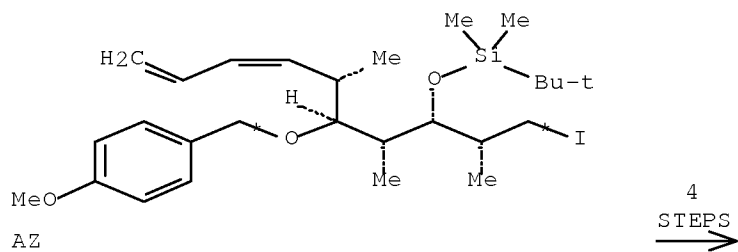
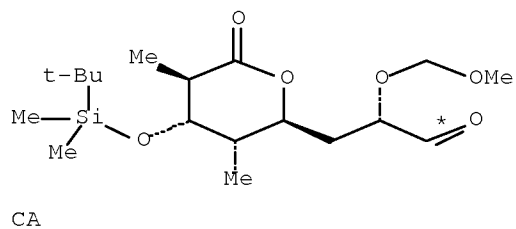
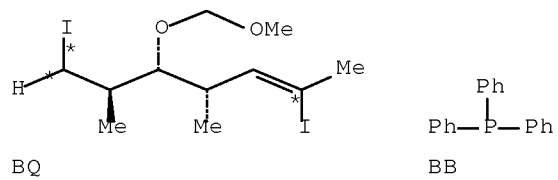
RX(22) RCT CC 852049-59-3

STAGE(1)
RGT BG 84-58-2 DDQ
SOL 7732-18-5 Water, 75-09-2 CH2Cl2
CON SUBSTAGE(1) 30 minutes, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature
SUBSTAGE(3) 15 minutes, room temperature

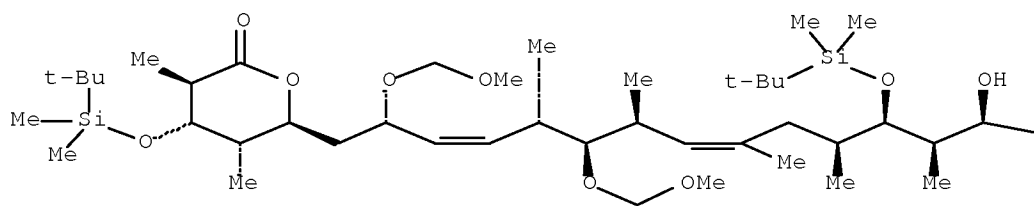
STAGE(2)
RGT BH 144-55-8 NaHCO3
SOL 7732-18-5 Water
CON room temperature

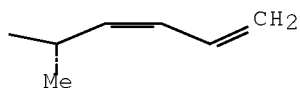
PRO CD 852049-60-6

RX(87) OF 178 COMPOSED OF RX(15), RX(20), RX(21), RX(22)
RX(87) BQ + BB + CA + AZ ==> CD



PAGE 1-A





CD
YIELD 91%

RX(15) RCT BQ 850211-71-1, BB 603-35-0
PRO BR 850211-72-2
CON SUBSTAGE(1) room temperature -> 95 deg C
SUBSTAGE(2) 18 hours, 95 deg C

RX(20) RCT BR 850211-72-2

STAGE(1)

RGT BU 1070-89-9 (Me3Si)2N.Na
SOL 109-99-9 THF
CON 1 hour, -78 deg C

STAGE(2)

RCT CA 852049-57-1
SOL 109-99-9 THF
CON SUBSTAGE(1) 2 hours, -78 deg C
SUBSTAGE(2) -78 deg C -> -10 deg C
SUBSTAGE(3) 2 hours, -10 deg C

STAGE(3)

RGT AJ 12125-02-9 NH4Cl
SOL 7732-18-5 Water, 60-29-7 Et2O

PRO CB 852049-58-2

RX(21) RCT AZ 850211-69-7

STAGE(1)

RGT BM 750545-03-0 Borate(1-),
1,5-cyclooctanediylhydromethoxy-, (T-4)-, AS 594-19-4
t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> room temperature
SUBSTAGE(3) 1 hour, room temperature

STAGE(2)

RCT CB 852049-58-2
RGT BW 603-32-7 Ph3As, BN 534-17-8 Cs2CO3
CAT 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

PRO CC 852049-59-3

RX(22) RCT CC 852049-59-3

STAGE(1)

RGT BG 84-58-2 DDQ

SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂

CON SUBSTAGE(1) 30 minutes, 0 deg C

SUBSTAGE(2) 0 deg C -> room temperature

SUBSTAGE(3) 15 minutes, room temperature

STAGE(2)

RGT BH 144-55-8 NaHCO₃

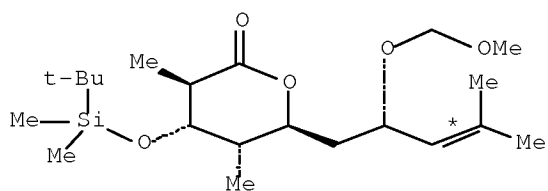
SOL 7732-18-5 Water

CON room temperature

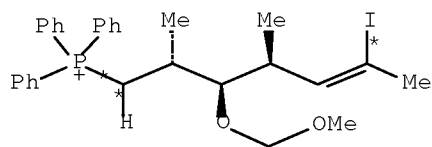
PRO CD 852049-60-6

RX(88) OF 178 COMPOSED OF RX(19), RX(20), RX(21), RX(22)

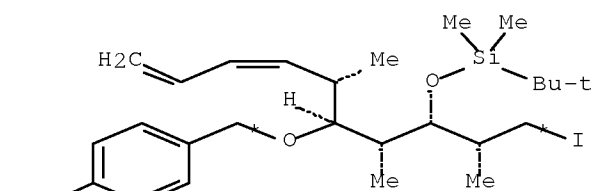
RX(88) BZ + BR + AZ ==> CD



BZ

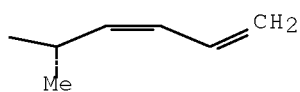
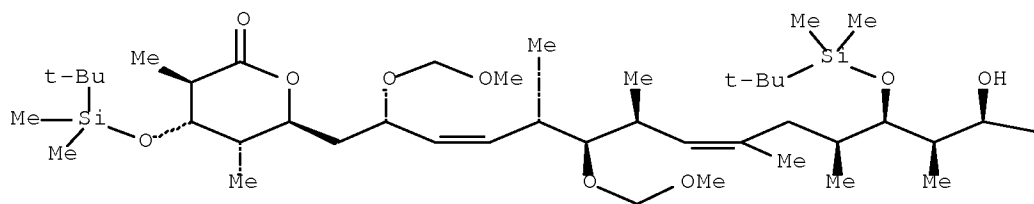


BR



AZ

4
STEPS
→



CD
YIELD 91%

RX(19) RCT BZ 852049-62-8

STAGE(1)

RGT AM 7782-44-7 O2, AN 10028-15-6 Ozone
SOL 75-09-2 CH2Cl2
CON -78 deg C

STAGE(2)

RGT BB 603-35-0 PPh3
CON 1 hour, room temperature

PRO CA 852049-57-1

RX(20) RCT BR 850211-72-2

STAGE(1)

RGT BU 1070-89-9 (Me3Si)2N.Na
SOL 109-99-9 THF
CON 1 hour, -78 deg C

STAGE(2)

RCT CA 852049-57-1
SOL 109-99-9 THF
CON SUBSTAGE(1) 2 hours, -78 deg C
SUBSTAGE(2) -78 deg C -> -10 deg C
SUBSTAGE(3) 2 hours, -10 deg C

STAGE(3)

RGT AJ 12125-02-9 NH4Cl
SOL 7732-18-5 Water, 60-29-7 Et2O

PRO CB 852049-58-2

RX(21) RCT AZ 850211-69-7

STAGE(1)

RGT BM 750545-03-0 Borate(1-),
1,5-cyclooctanediylhydromethoxy-, (T-4)-, AS 594-19-4
t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> room temperature
SUBSTAGE(3) 1 hour, room temperature

STAGE(2)

RCT CB 852049-58-2
RGT BW 603-32-7 Ph3As, BN 534-17-8 Cs2CO3
CAT 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

PRO CC 852049-59-3

RX(22) RCT CC 852049-59-3

STAGE(1)

RGT BG 84-58-2 DDQ
SOL 7732-18-5 Water, 75-09-2 CH2Cl2
CON SUBSTAGE(1) 30 minutes, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature
SUBSTAGE(3) 15 minutes, room temperature

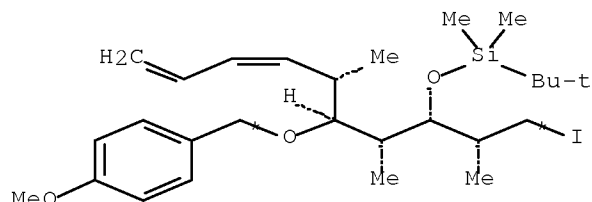
STAGE(2)

RGT BH 144-55-8 NaHCO3
SOL 7732-18-5 Water
CON room temperature

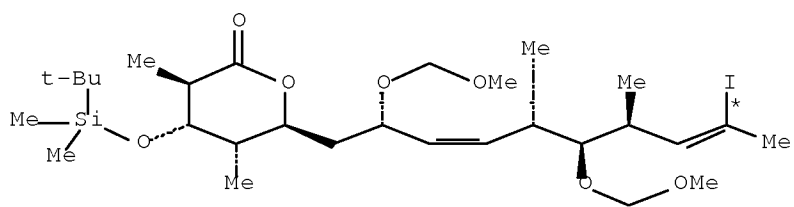
PRO CD 852049-60-6

RX(89) OF 178 COMPOSED OF RX(21), RX(22), RX(23)

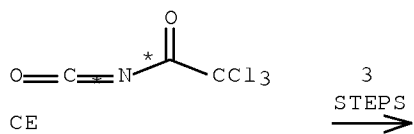
RX(89) AZ + CE + CE ==> CF



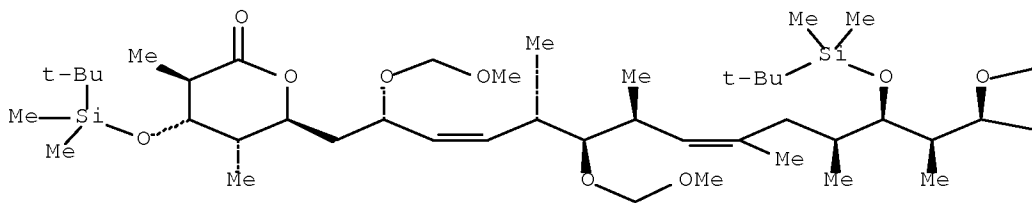
AZ



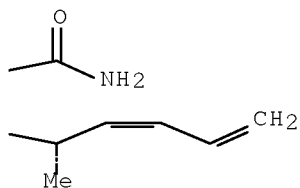
CB



PAGE 1-A



PAGE 1-B



CF
YIELD 92%

RX(21) RCT AZ 850211-69-7

STAGE(1)

RGT BM 750545-03-0 Borate(1-),
1,5-cyclooctanediylhydromethoxy-, (T-4)-, AS 594-19-4
t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0

Pentane
 CON SUBSTAGE(1) -78 deg C
 SUBSTAGE(2) -78 deg C -> room temperature
 SUBSTAGE(3) 1 hour, room temperature

STAGE(2)
 RCT CB 852049-58-2
 RGT BW 603-32-7 Ph3As, BN 534-17-8 Cs2CO3
 CAT 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

PRO CC 852049-59-3

RX(22) RCT CC 852049-59-3

STAGE(1)
 RGT BG 84-58-2 DDQ
 SOL 7732-18-5 Water, 75-09-2 CH2Cl2
 CON SUBSTAGE(1) 30 minutes, 0 deg C
 SUBSTAGE(2) 0 deg C -> room temperature
 SUBSTAGE(3) 15 minutes, room temperature

STAGE(2)
 RGT BH 144-55-8 NaHCO3
 SOL 7732-18-5 Water
 CON room temperature

PRO CD 852049-60-6

RX(23) RCT CD 852049-60-6, CE 3019-71-4

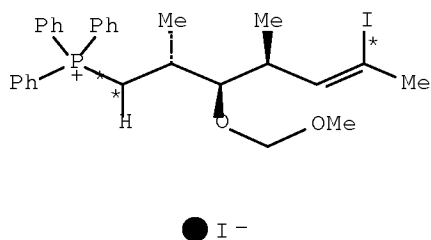
STAGE(1)
 SOL 75-09-2 CH2Cl2, 108-88-3 PhMe
 CON 30 minutes, room temperature

STAGE(2)
 RGT CG 1344-28-1 Al2O3
 CON 4 hours, room temperature

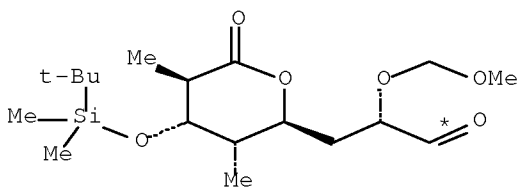
PRO CF 852049-61-7

RX(91) OF 178 COMPOSED OF RX(20), RX(21), RX(22), RX(23)

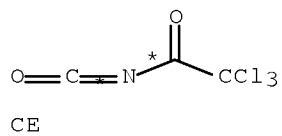
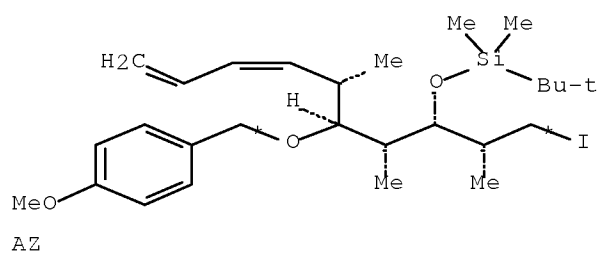
RX(91) BR + CA + AZ + CE ==> CF



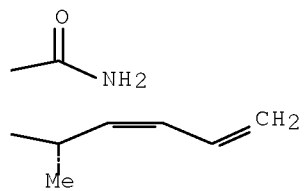
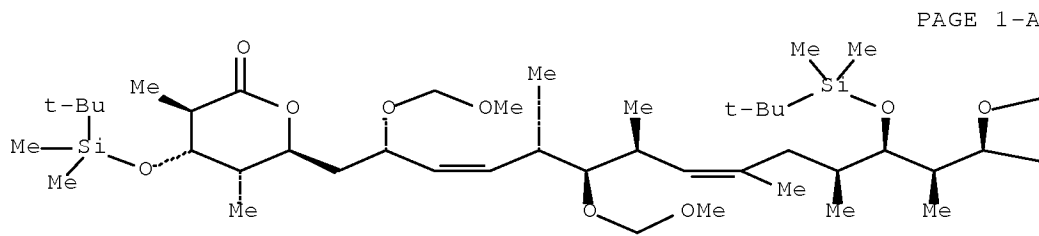
BR



CA



4
STEPS
→



CF
YIELD 92%

PAGE 1-B

RX(20) RCT BR 850211-72-2

STAGE(1)

RGT BU 1070-89-9 (Me3Si)2N.Na

SOL 109-99-9 THF
CON 1 hour, -78 deg C

STAGE(2)

RCT CA 852049-57-1
SOL 109-99-9 THF
CON SUBSTAGE(1) 2 hours, -78 deg C
SUBSTAGE(2) -78 deg C -> -10 deg C
SUBSTAGE(3) 2 hours, -10 deg C

STAGE(3)

RGT AJ 12125-02-9 NH4Cl
SOL 7732-18-5 Water, 60-29-7 Et2O

PRO CB 852049-58-2

RX(21) RCT AZ 850211-69-7

STAGE(1)

RGT BM 750545-03-0 Borate(1-),
1,5-cyclooctanediylhydromethoxy-, (T-4)-, AS 594-19-4
t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> room temperature
SUBSTAGE(3) 1 hour, room temperature

STAGE(2)

RCT CB 852049-58-2
RGT BW 603-32-7 Ph3As, BN 534-17-8 Cs2CO3
CAT 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

PRO CC 852049-59-3

RX(22) RCT CC 852049-59-3

STAGE(1)

RGT BG 84-58-2 DDQ
SOL 7732-18-5 Water, 75-09-2 CH2Cl2
CON SUBSTAGE(1) 30 minutes, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature
SUBSTAGE(3) 15 minutes, room temperature

STAGE(2)

RGT BH 144-55-8 NaHCO3
SOL 7732-18-5 Water
CON room temperature

PRO CD 852049-60-6

RX(23) RCT CD 852049-60-6, CE 3019-71-4

STAGE(1)

SOL 75-09-2 CH2Cl2, 108-88-3 PhMe
CON 30 minutes, room temperature

STAGE(2)

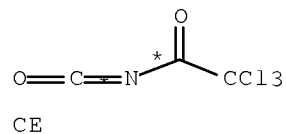
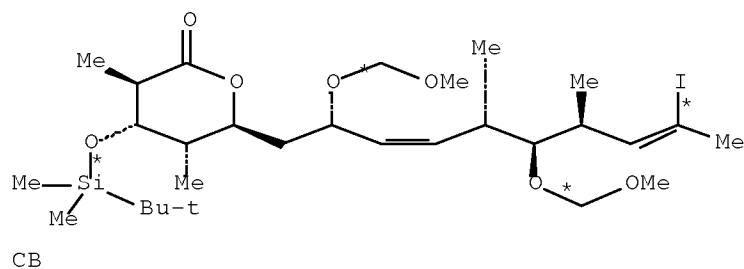
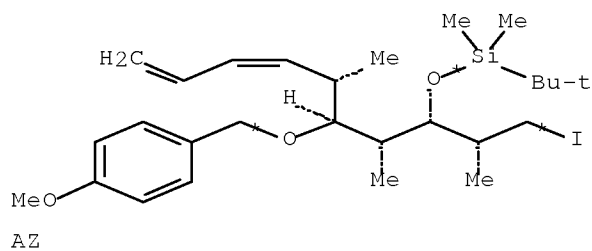
RGT CG 1344-28-1 Al2O3

CON 4 hours, room temperature

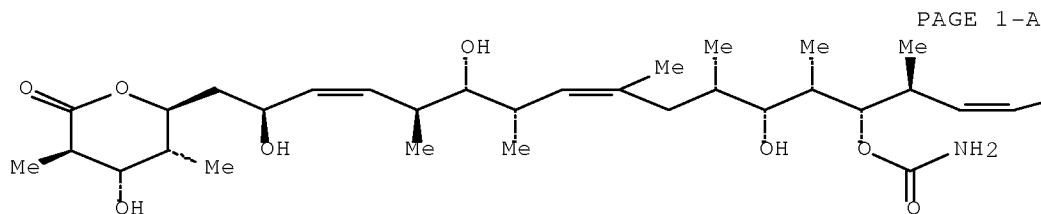
PRO CF 852049-61-7

RX(93) OF 178 COMPOSED OF RX(21), RX(22), RX(23), RX(24)

RX(93) AZ + CB + CE ==> CI



4
STEPS
→





CI
YIELD 95%

RX(21) RCT AZ 850211-69-7

STAGE(1)

RGT BM 750545-03-0 Borate(1-),
1,5-cyclooctanediylhydromethoxy-, (T-4)-, AS 594-19-4
t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> room temperature
SUBSTAGE(3) 1 hour, room temperature

STAGE(2)

RCT CB 852049-58-2
RGT BW 603-32-7 Ph3As, BN 534-17-8 Cs2CO3
CAT 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

PRO CC 852049-59-3

RX(22) RCT CC 852049-59-3

STAGE(1)

RGT BG 84-58-2 DDQ
SOL 7732-18-5 Water, 75-09-2 CH2Cl2
CON SUBSTAGE(1) 30 minutes, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature
SUBSTAGE(3) 15 minutes, room temperature

STAGE(2)

RGT BH 144-55-8 NaHCO3
SOL 7732-18-5 Water
CON room temperature

PRO CD 852049-60-6

RX(23) RCT CD 852049-60-6, CE 3019-71-4

STAGE(1)

SOL 75-09-2 CH2Cl2, 108-88-3 PhMe
CON 30 minutes, room temperature

STAGE(2)

RGT CG 1344-28-1 Al2O3
CON 4 hours, room temperature

PRO CF 852049-61-7

RX(24) RCT CF 852049-61-7

STAGE(1)

RGT CJ 7647-01-0 HCl
SOL 7732-18-5 Water, 67-56-1 MeOH
CON SUBSTAGE(1) 15 minutes, room temperature
SUBSTAGE(2) 6 hours, room temperature

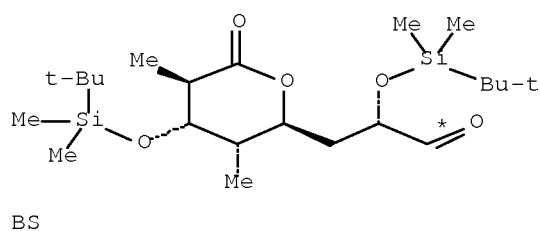
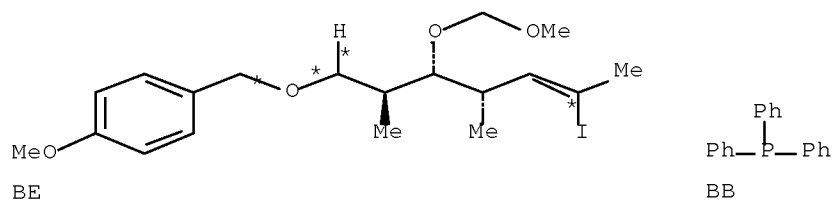
STAGE(2)

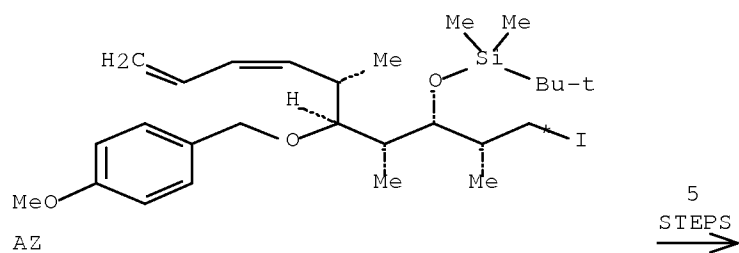
RGT BH 144-55-8 NaHCO3
CON room temperature

PRO CI 127943-53-7

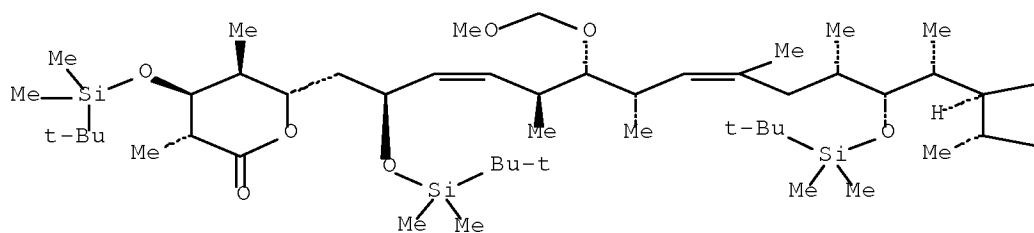
RX(136) OF 178 COMPOSED OF RX(11), RX(14), RX(15), RX(16), RX(17)

RX(136) BE + BB + BS + AZ ==> BV

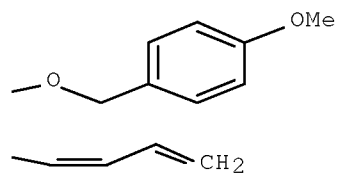




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PAGE 1-B



BV
 YIELD 40%

RX(11) RCT BE 633294-02-7

STAGE(1)

RGT BG 84-58-2 DDQ

SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂

CON 2 hours, 0 deg C

STAGE(2)

RGT BH 144-55-8 NaHCO₃

SOL 7732-18-5 Water

PRO BF 850211-70-0

RX(14) RCT BF 850211-70-0

STAGE(1)

RGT BA 7553-56-2 I2, BB 603-35-0 PPh3, BC 288-32-4 1H-Imidazole
SOL 60-29-7 Et2O, 71-43-2 Benzene
CON SUBSTAGE(1) 0 deg C -> room temperature
SUBSTAGE(2) 12 hours, room temperature

STAGE(2)

RGT BH 144-55-8 NaHCO3
SOL 7732-18-5 Water
CON room temperature

PRO BQ 850211-71-1

RX(15) RCT BQ 850211-71-1, BB 603-35-0
PRO BR 850211-72-2
CON SUBSTAGE(1) room temperature -> 95 deg C
SUBSTAGE(2) 18 hours, 95 deg C

RX(16) RCT BR 850211-72-2

STAGE(1)

RGT BU 1070-89-9 (Me3Si)2N.Na
SOL 109-99-9 THF
CON 1 hour, -78 deg C

STAGE(2)

RCT BS 252342-51-1
SOL 109-99-9 THF
CON SUBSTAGE(1) 2 hours, -78 deg C
SUBSTAGE(2) -78 deg C -> -10 deg C
SUBSTAGE(3) 2 hours, -10 deg C

STAGE(3)

RGT AJ 12125-02-9 NH4Cl
SOL 7732-18-5 Water, 60-29-7 Et2O

PRO BT 850211-74-4

RX(17) RCT AZ 850211-69-7

STAGE(1)

RGT BM 750545-03-0 Borate(1-),
1,5-cyclooctanediylhydromethoxy-, (T-4)-, AS 594-19-4
t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> room temperature
SUBSTAGE(3) 1 hour, room temperature

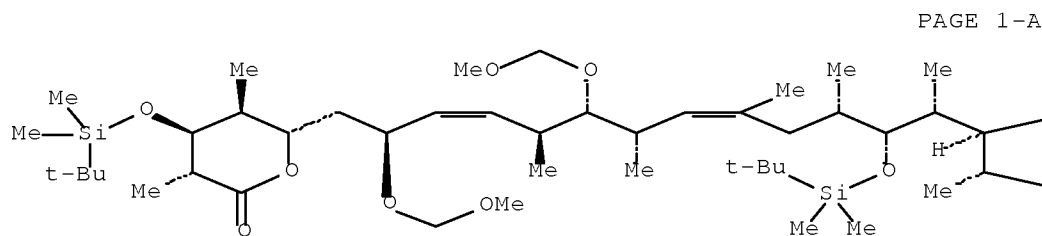
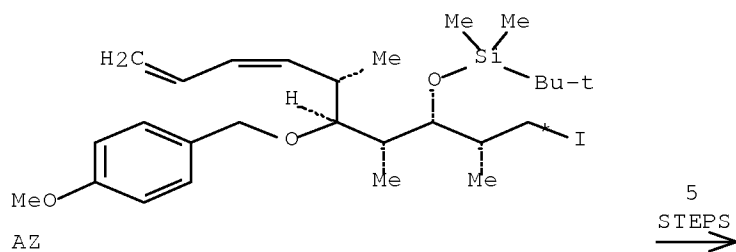
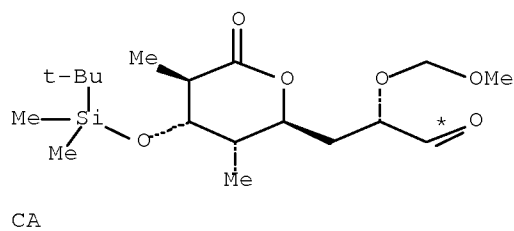
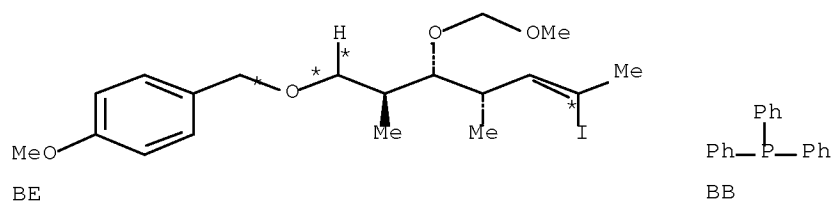
STAGE(2)

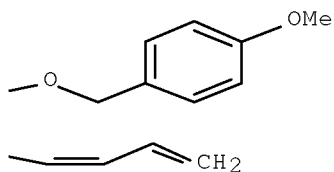
RCT BT 850211-74-4
RGT BW 603-32-7 Ph3As, BN 534-17-8 Cs2CO3
CAT 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water
CON 20 hours, room temperature

PRO BV 633293-75-1

NTE in the dark

RX(137) OF 178 COMPOSED OF RX(11), RX(14), RX(15), RX(20), RX(21)
RX(137) BE + BB + CA + AZ ==> CC





CC
YIELD 60%

RX(11) RCT BE 633294-02-7

STAGE(1)

RGT BG 84-58-2 DDQ
SOL 7732-18-5 Water, 75-09-2 CH2Cl2
CON 2 hours, 0 deg C

STAGE(2)

RGT BH 144-55-8 NaHCO3
SOL 7732-18-5 Water

PRO BF 850211-70-0

RX(14) RCT BF 850211-70-0

STAGE(1)

RGT BA 7553-56-2 I2, BB 603-35-0 PPh3, BC 288-32-4 1H-Imidazole
SOL 60-29-7 Et2O, 71-43-2 Benzene
CON SUBSTAGE(1) 0 deg C -> room temperature
SUBSTAGE(2) 12 hours, room temperature

STAGE(2)

RGT BH 144-55-8 NaHCO3
SOL 7732-18-5 Water
CON room temperature

PRO BQ 850211-71-1

RX(15) RCT BQ 850211-71-1, BB 603-35-0
PRO BR 850211-72-2
CON SUBSTAGE(1) room temperature -> 95 deg C
SUBSTAGE(2) 18 hours, 95 deg C

RX(20) RCT BR 850211-72-2

STAGE(1)

RGT BU 1070-89-9 (Me3Si)2N.Na
SOL 109-99-9 THF
CON 1 hour, -78 deg C

STAGE(2)

RCT CA 852049-57-1
SOL 109-99-9 THF
CON SUBSTAGE(1) 2 hours, -78 deg C
SUBSTAGE(2) -78 deg C -> -10 deg C

SUBSTAGE(3) 2 hours, -10 deg C

STAGE(3)

RGT AJ 12125-02-9 NH4Cl

SOL 7732-18-5 Water, 60-29-7 Et2O

PRO CB 852049-58-2

RX(21) RCT AZ 850211-69-7

STAGE(1)

RGT BM 750545-03-0 Borate(1-),

1,5-cyclooctanediylhydromethoxy-, (T-4)-, AS 594-19-4
t-BuLi

SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane

CON SUBSTAGE(1) -78 deg C

SUBSTAGE(2) -78 deg C -> room temperature

SUBSTAGE(3) 1 hour, room temperature

STAGE(2)

RCT CB 852049-58-2

RGT BW 603-32-7 Ph3As, BN 534-17-8 Cs2CO3

CAT 72287-26-4 Palladium,

[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-

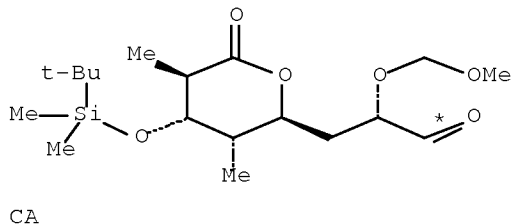
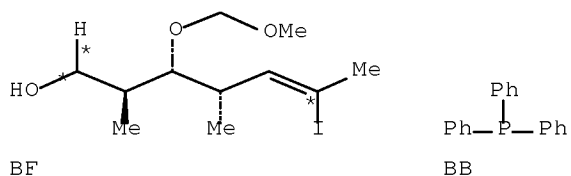
SOL 7732-18-5 Water, 68-12-2 DMF

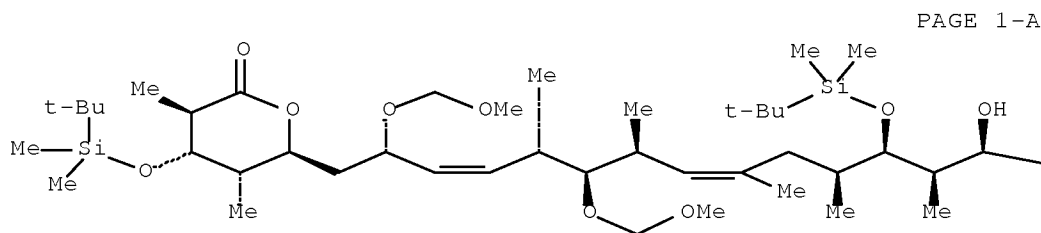
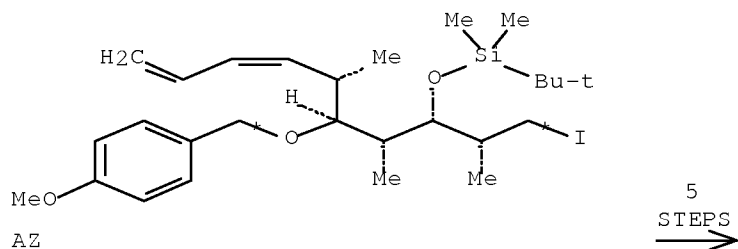
CON 20 hours, room temperature

PRO CC 852049-59-3

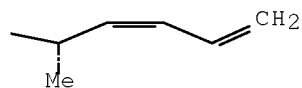
RX(138) OF 178 COMPOSED OF RX(14), RX(15), RX(20), RX(21), RX(22)

RX(138) EF + BB + CA + AZ ==> CD





PAGE 1-B



CD
 YIELD 91%

RX(14) RCT BF 850211-70-0

STAGE(1)

RGT BA 7553-56-2 I2, BB 603-35-0 PPh3, BC 288-32-4 1H-Imidazole
 SOL 60-29-7 Et2O, 71-43-2 Benzene
 CON SUBSTAGE(1) 0 deg C -> room temperature
 SUBSTAGE(2) 12 hours, room temperature

STAGE(2)

RGT BH 144-55-8 NaHCO3
 SOL 7732-18-5 Water
 CON room temperature

PRO BQ 850211-71-1

RX(15) RCT BQ 850211-71-1, BB 603-35-0

PRO BR 850211-72-2
CON SUBSTAGE(1) room temperature -> 95 deg C
SUBSTAGE(2) 18 hours, 95 deg C

RX(20) RCT BR 850211-72-2

STAGE(1)
RGT BU 1070-89-9 (Me3Si)2N.Na
SOL 109-99-9 THF
CON 1 hour, -78 deg C

STAGE(2)
RCT CA 852049-57-1
SOL 109-99-9 THF
CON SUBSTAGE(1) 2 hours, -78 deg C
SUBSTAGE(2) -78 deg C -> -10 deg C
SUBSTAGE(3) 2 hours, -10 deg C

STAGE(3)
RGT AJ 12125-02-9 NH4Cl
SOL 7732-18-5 Water, 60-29-7 Et2O

PRO CB 852049-58-2

RX(21) RCT AZ 850211-69-7

STAGE(1)
RGT BM 750545-03-0 Borate(1-),
1,5-cyclooctanediylhydromethoxy-, (T-4)-, AS 594-19-4
t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> room temperature
SUBSTAGE(3) 1 hour, room temperature

STAGE(2)
RCT CB 852049-58-2
RGT BW 603-32-7 Ph3As, BN 534-17-8 Cs2CO3
CAT 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

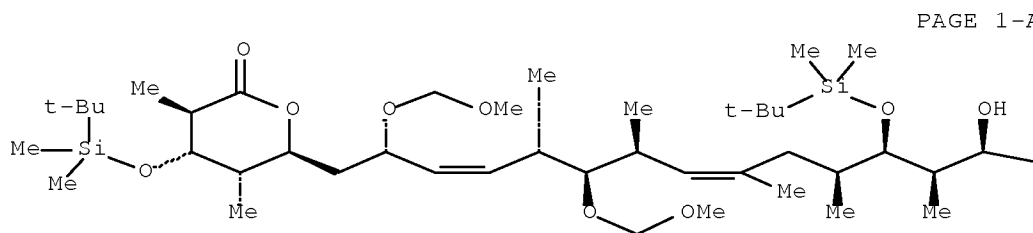
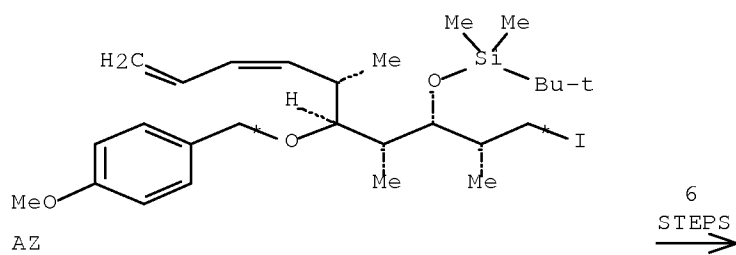
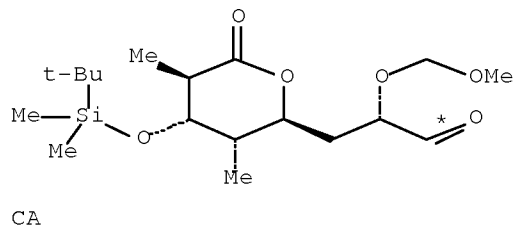
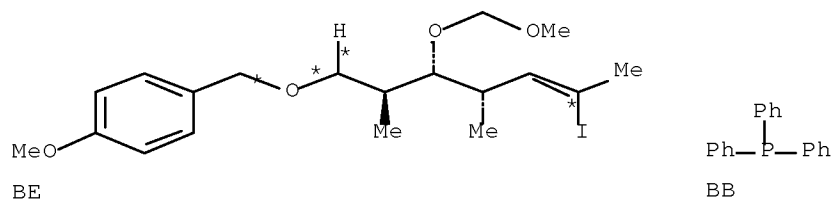
PRO CC 852049-59-3

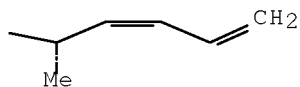
RX(22) RCT CC 852049-59-3

STAGE(1)
RGT BG 84-58-2 DDQ
SOL 7732-18-5 Water, 75-09-2 CH2Cl2
CON SUBSTAGE(1) 30 minutes, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature
SUBSTAGE(3) 15 minutes, room temperature

STAGE(2)
RGT BH 144-55-8 NaHCO3
SOL 7732-18-5 Water
CON room temperature

RX(139) OF 178 COMPOSED OF RX(11), RX(14), RX(15), RX(20), RX(21), RX(22)
 RX(139) EE + BB + CA + AZ ==> CD





CD
YIELD 91%

RX(11) RCT BE 633294-02-7

STAGE(1)

RGT BG 84-58-2 DDQ
SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
CON 2 hours, 0 deg C

STAGE(2)

RGT BH 144-55-8 NaHCO₃
SOL 7732-18-5 Water

PRO BF 850211-70-0

RX(14) RCT BF 850211-70-0

STAGE(1)

RGT BA 7553-56-2 I₂, BB 603-35-0 PPh₃, BC 288-32-4 1H-Imidazole
SOL 60-29-7 Et₂O, 71-43-2 Benzene
CON SUBSTAGE(1) 0 deg C -> room temperature
SUBSTAGE(2) 12 hours, room temperature

STAGE(2)

RGT BH 144-55-8 NaHCO₃
SOL 7732-18-5 Water
CON room temperature

PRO BQ 850211-71-1

RX(15) RCT BQ 850211-71-1, BB 603-35-0
PRO BR 850211-72-2
CON SUBSTAGE(1) room temperature -> 95 deg C
SUBSTAGE(2) 18 hours, 95 deg C

RX(20) RCT BR 850211-72-2

STAGE(1)

RGT BU 1070-89-9 (Me₃Si)₂N.Na
SOL 109-99-9 THF
CON 1 hour, -78 deg C

STAGE(2)

RCT CA 852049-57-1
SOL 109-99-9 THF

CON SUBSTAGE(1) 2 hours, -78 deg C
SUBSTAGE(2) -78 deg C -> -10 deg C
SUBSTAGE(3) 2 hours, -10 deg C

STAGE(3)

RGT AJ 12125-02-9 NH4Cl
SOL 7732-18-5 Water, 60-29-7 Et2O

PRO CB 852049-58-2

RX(21) RCT AZ 850211-69-7

STAGE(1)

RGT BM 750545-03-0 Borate(1-),
1,5-cyclooctanediylhydromethoxy-, (T-4)-, AS 594-19-4
t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> room temperature
SUBSTAGE(3) 1 hour, room temperature

STAGE(2)

RCT CB 852049-58-2
RGT BW 603-32-7 Ph3As, BN 534-17-8 Cs2CO3
CAT 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

PRO CC 852049-59-3

RX(22) RCT CC 852049-59-3

STAGE(1)

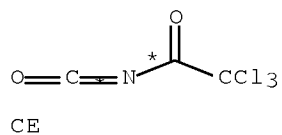
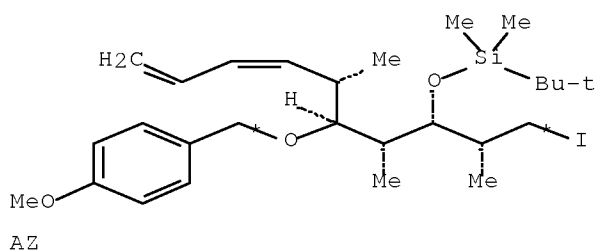
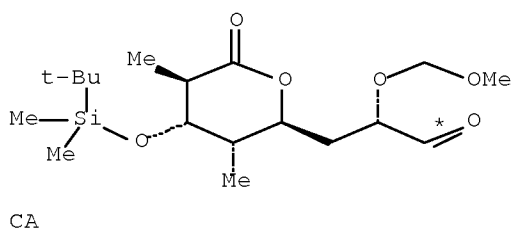
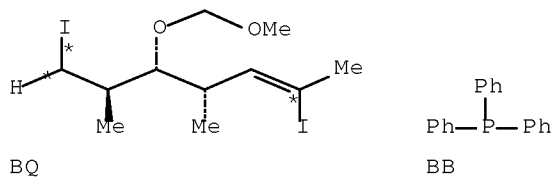
RGT BG 84-58-2 DDQ
SOL 7732-18-5 Water, 75-09-2 CH2Cl2
CON SUBSTAGE(1) 30 minutes, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature
SUBSTAGE(3) 15 minutes, room temperature

STAGE(2)

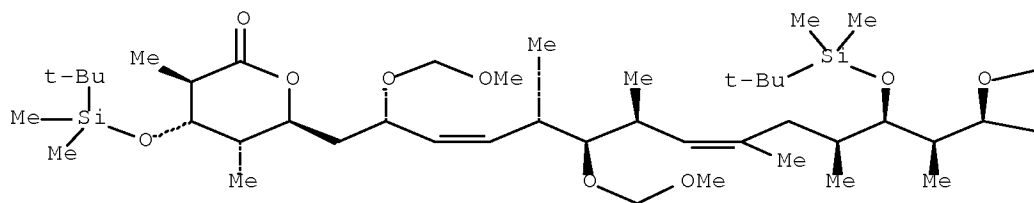
RGT BH 144-55-8 NaHCO3
SOL 7732-18-5 Water
CON room temperature

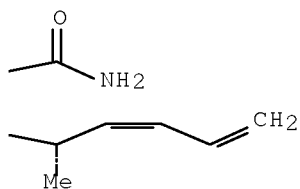
PRO CD 852049-60-6

RX(140) OF 178 COMPOSED OF RX(15), RX(20), RX(21), RX(22), RX(23)
RX(140) EQ + BB + CA + AZ + CE ==> CF



5
STEPS
→





CF
YIELD 92%

RX(15) RCT BQ 850211-71-1, BB 603-35-0
PRO BR 850211-72-2
CON SUBSTAGE(1) room temperature -> 95 deg C
SUBSTAGE(2) 18 hours, 95 deg C

RX(20) RCT BR 850211-72-2

STAGE(1)

RGT BU 1070-89-9 (Me3Si)2N.Na
SOL 109-99-9 THF
CON 1 hour, -78 deg C

STAGE(2)

RCT CA 852049-57-1
SOL 109-99-9 THF
CON SUBSTAGE(1) 2 hours, -78 deg C
SUBSTAGE(2) -78 deg C -> -10 deg C
SUBSTAGE(3) 2 hours, -10 deg C

STAGE(3)

RGT AJ 12125-02-9 NH4Cl
SOL 7732-18-5 Water, 60-29-7 Et2O

PRO CB 852049-58-2

RX(21) RCT AZ 850211-69-7

STAGE(1)

RGT BM 750545-03-0 Borate(1-),
1,5-cyclooctanediylhydromethoxy-, (T-4)-, AS 594-19-4
t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> room temperature
SUBSTAGE(3) 1 hour, room temperature

STAGE(2)

RCT CB 852049-58-2
RGT BW 603-32-7 Ph3As, BN 534-17-8 Cs2CO3
CAT 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-

SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

PRO CC 852049-59-3

RX(22) RCT CC 852049-59-3

STAGE(1)

RGT BG 84-58-2 DDQ
SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
CON SUBSTAGE(1) 30 minutes, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature
SUBSTAGE(3) 15 minutes, room temperature

STAGE(2)

RGT BH 144-55-8 NaHCO₃
SOL 7732-18-5 Water
CON room temperature

PRO CD 852049-60-6

RX(23) RCT CD 852049-60-6, CE 3019-71-4

STAGE(1)

SOL 75-09-2 CH₂Cl₂, 108-88-3 PhMe
CON 30 minutes, room temperature

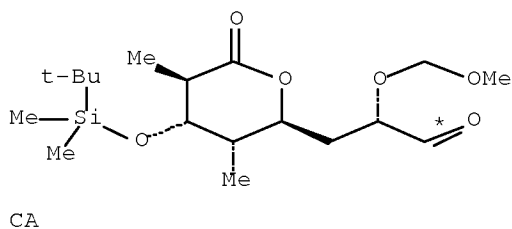
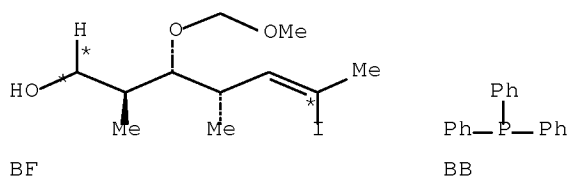
STAGE(2)

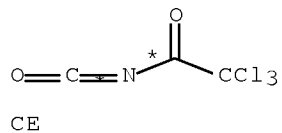
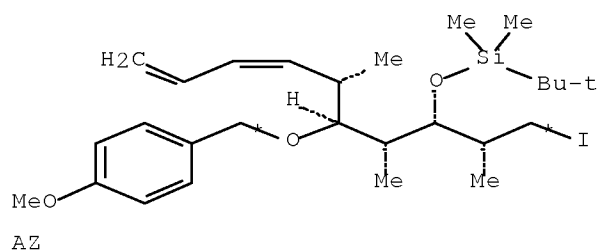
RGT CG 1344-28-1 Al₂O₃
CON 4 hours, room temperature

PRO CF 852049-61-7

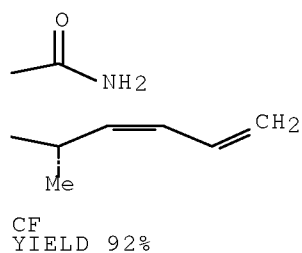
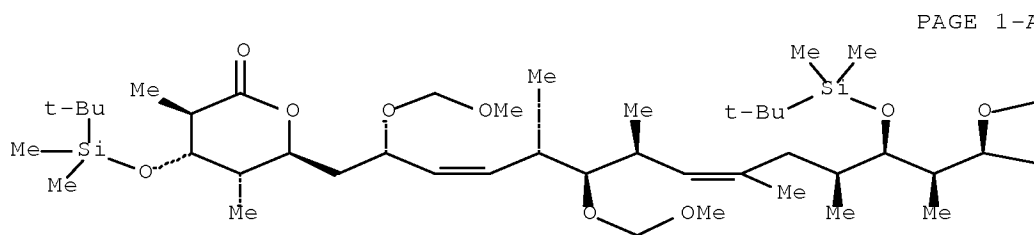
RX(141) OF 178 COMPOSED OF RX(14), RX(15), RX(20), RX(21), RX(22), RX(23)

RX(141) BF + BB + CA + AZ + CE ==> CF





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 STEPS



PAGE 1-B

RX(14) RCT BF 850211-70-0

STAGE(1)

RGT BA 7553-56-2 I2, BB 603-35-0 PPh3, BC 288-32-4 1H-Imidazole
 SOL 60-29-7 Et2O, 71-43-2 Benzene

CON SUBSTAGE(1) 0 deg C -> room temperature
 SUBSTAGE(2) 12 hours, room temperature

STAGE(2)
 RGT BH 144-55-8 NaHCO₃
 SOL 7732-18-5 Water
 CON room temperature

PRO BQ 850211-71-1

RX(15) RCT BQ 850211-71-1, BB 603-35-0
 PRO BR 850211-72-2
 CON SUBSTAGE(1) room temperature -> 95 deg C
 SUBSTAGE(2) 18 hours, 95 deg C

RX(20) RCT BR 850211-72-2

STAGE(1)
 RGT BU 1070-89-9 (Me₃Si)₂N.Na
 SOL 109-99-9 THF
 CON 1 hour, -78 deg C

STAGE(2)
 RCT CA 852049-57-1
 SOL 109-99-9 THF
 CON SUBSTAGE(1) 2 hours, -78 deg C
 SUBSTAGE(2) -78 deg C -> -10 deg C
 SUBSTAGE(3) 2 hours, -10 deg C

STAGE(3)
 RGT AJ 12125-02-9 NH₄Cl
 SOL 7732-18-5 Water, 60-29-7 Et₂O

PRO CB 852049-58-2

RX(21) RCT AZ 850211-69-7

STAGE(1)
 RGT BM 750545-03-0 Borate(1-),
 1,5-cyclooctanediylhydromethoxy-, (T-4)-, AS 594-19-4
 t-BuLi
 SOL 60-29-7 Et₂O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
 Pentane
 CON SUBSTAGE(1) -78 deg C
 SUBSTAGE(2) -78 deg C -> room temperature
 SUBSTAGE(3) 1 hour, room temperature

STAGE(2)
 RCT CB 852049-58-2
 RGT BW 603-32-7 Ph₃As, BN 534-17-8 Cs₂CO₃
 CAT 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

PRO CC 852049-59-3

RX(22) RCT CC 852049-59-3

STAGE(1)

RGT BG 84-58-2 DDQ
 SOL 7732-18-5 Water, 75-09-2 CH2Cl2
 CON SUBSTAGE(1) 30 minutes, 0 deg C
 SUBSTAGE(2) 0 deg C -> room temperature
 SUBSTAGE(3) 15 minutes, room temperature

STAGE(2)

RGT BH 144-55-8 NaHCO3
 SOL 7732-18-5 Water
 CON room temperature

PRO CD 852049-60-6

RX(23) RCT CD 852049-60-6, CE 3019-71-4

STAGE(1)

SOL 75-09-2 CH2Cl2, 108-88-3 PhMe
 CON 30 minutes, room temperature

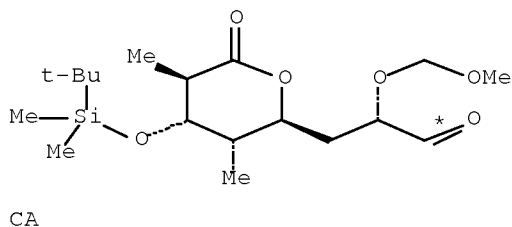
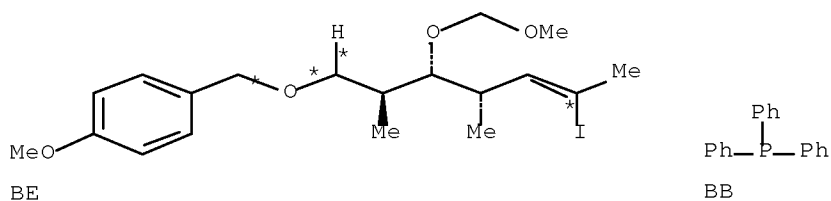
STAGE(2)

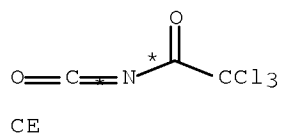
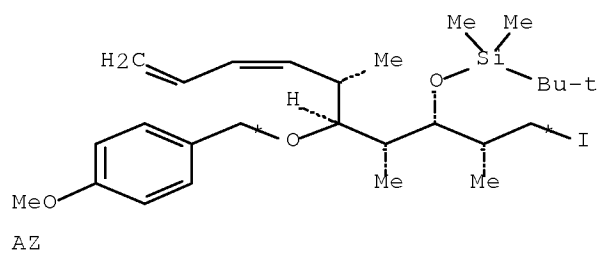
RGT CG 1344-28-1 Al2O3
 CON 4 hours, room temperature

PRO CF 852049-61-7

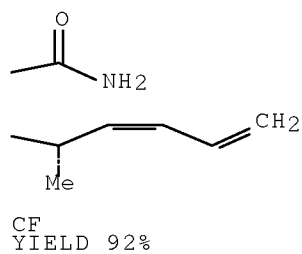
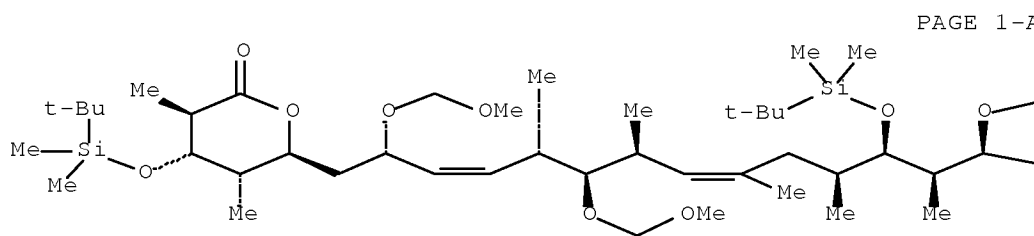
RX(142) OF 178 COMPOSED OF RX(11), RX(14), RX(15), RX(20), RX(21), RX(22),
 RX(23)

RX(142) BE + BB + CA + AZ + CE ==> CF





7
 STEPS



PAGE 1-B

RX(11) RCT BE 633294-02-7

STAGE(1)

RGT BG 84-58-2 DDQ

SOL 7732-18-5 Water, 75-09-2 CH2Cl2

CON 2 hours, 0 deg C

STAGE(2)

RGT BH 144-55-8 NaHCO₃
 SOL 7732-18-5 Water

 PRO BF 850211-70-0

 RX(14) RCT BF 850211-70-0

 STAGE(1)
 RGT BA 7553-56-2 I₂, BB 603-35-0 PPh₃, BC 288-32-4 1H-Imidazole
 SOL 60-29-7 Et₂O, 71-43-2 Benzene
 CON SUBSTAGE(1) 0 deg C -> room temperature
 SUBSTAGE(2) 12 hours, room temperature

 STAGE(2)
 RGT BH 144-55-8 NaHCO₃
 SOL 7732-18-5 Water
 CON room temperature

 PRO BQ 850211-71-1

 RX(15) RCT BQ 850211-71-1, BB 603-35-0
 PRO BR 850211-72-2
 CON SUBSTAGE(1) room temperature -> 95 deg C
 SUBSTAGE(2) 18 hours, 95 deg C

 RX(20) RCT BR 850211-72-2

 STAGE(1)
 RGT BU 1070-89-9 (Me₃Si)₂N.Na
 SOL 109-99-9 THF
 CON 1 hour, -78 deg C

 STAGE(2)
 RCT CA 852049-57-1
 SOL 109-99-9 THF
 CON SUBSTAGE(1) 2 hours, -78 deg C
 SUBSTAGE(2) -78 deg C -> -10 deg C
 SUBSTAGE(3) 2 hours, -10 deg C

 STAGE(3)
 RGT AJ 12125-02-9 NH₄Cl
 SOL 7732-18-5 Water, 60-29-7 Et₂O

 PRO CB 852049-58-2

 RX(21) RCT AZ 850211-69-7

 STAGE(1)
 RGT BM 750545-03-0 Borate(1-),
 1,5-cyclooctanediylhydromethoxy-, (T-4)-, AS 594-19-4
 t-BuLi
 SOL 60-29-7 Et₂O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
 Pentane
 CON SUBSTAGE(1) -78 deg C
 SUBSTAGE(2) -78 deg C -> room temperature
 SUBSTAGE(3) 1 hour, room temperature

 STAGE(2)
 RCT CB 852049-58-2
 RGT BW 603-32-7 Ph₃As, BN 534-17-8 Cs₂CO₃

CAT 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

PRO CC 852049-59-3

RX(22) RCT CC 852049-59-3

STAGE(1)

RGT BG 84-58-2 DDQ
SOL 7732-18-5 Water, 75-09-2 CH2Cl2
CON SUBSTAGE(1) 30 minutes, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature
SUBSTAGE(3) 15 minutes, room temperature

STAGE(2)

RGT BH 144-55-8 NaHCO3
SOL 7732-18-5 Water
CON room temperature

PRO CD 852049-60-6

RX(23) RCT CD 852049-60-6, CE 3019-71-4

STAGE(1)

SOL 75-09-2 CH2Cl2, 108-88-3 PhMe
CON 30 minutes, room temperature

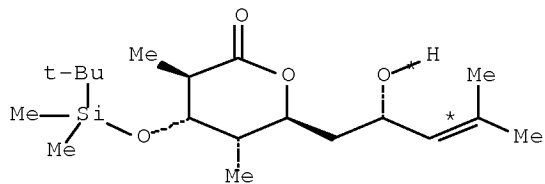
STAGE(2)

RGT CG 1344-28-1 Al2O3
CON 4 hours, room temperature

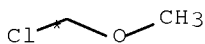
PRO CF 852049-61-7

RX(143) OF 178 COMPOSED OF RX(18), RX(19), RX(20), RX(21), RX(22)

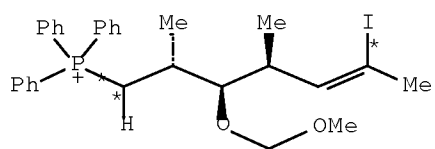
RX(143) BX + BY + BR + AZ ==> CD



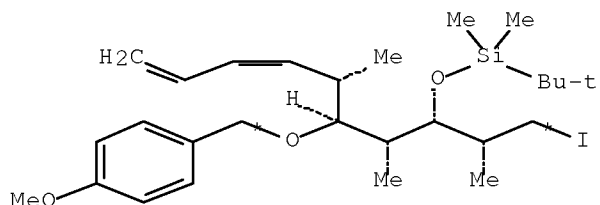
BX



BY

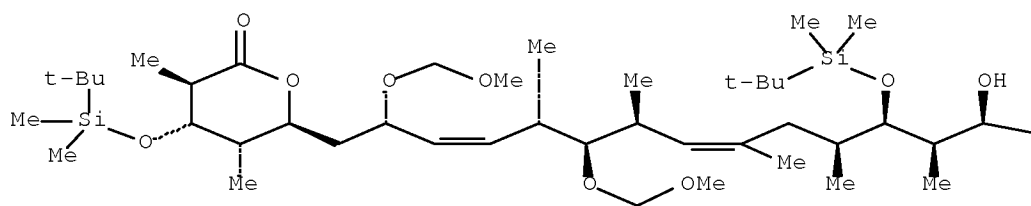


BR



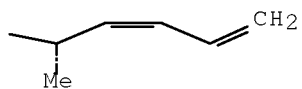
AZ

5
STEPS
→



PAGE 1-A

PAGE 1-B



CD
YIELD 91%

RX(18) RCT BX 256920-77-1, BY 107-30-2

STAGE(1)

RGT H 7087-68-5 EtN(Pr-i)2

SOL 75-09-2 CH2Cl2

CON 12 hours, room temperature

STAGE(2)

RGT BK 7647-14-5 NaCl
SOL 7732-18-5 Water
CON room temperature

PRO BZ 852049-62-8

RX(19) RCT BZ 852049-62-8

STAGE(1)

RGT AM 7782-44-7 O2, AN 10028-15-6 Ozone
SOL 75-09-2 CH2Cl2
CON -78 deg C

STAGE(2)

RGT BB 603-35-0 PPh3
CON 1 hour, room temperature

PRO CA 852049-57-1

RX(20) RCT BR 850211-72-2

STAGE(1)

RGT BU 1070-89-9 (Me3Si)2N.Na
SOL 109-99-9 THF
CON 1 hour, -78 deg C

STAGE(2)

RCT CA 852049-57-1
SOL 109-99-9 THF
CON SUBSTAGE(1) 2 hours, -78 deg C
SUBSTAGE(2) -78 deg C -> -10 deg C
SUBSTAGE(3) 2 hours, -10 deg C

STAGE(3)

RGT AJ 12125-02-9 NH4Cl
SOL 7732-18-5 Water, 60-29-7 Et2O

PRO CB 852049-58-2

RX(21) RCT AZ 850211-69-7

STAGE(1)

RGT BM 750545-03-0 Borate(1-),
1,5-cyclooctanediylhydromethoxy-, (T-4)-, AS 594-19-4
t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> room temperature
SUBSTAGE(3) 1 hour, room temperature

STAGE(2)

RCT CB 852049-58-2
RGT BW 603-32-7 Ph3As, BN 534-17-8 Cs2CO3
CAT 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

PRO CC 852049-59-3

RX(22) RCT CC 852049-59-3

STAGE(1)

RGT BG 84-58-2 DDQ

SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂

CON SUBSTAGE(1) 30 minutes, 0 deg C

SUBSTAGE(2) 0 deg C -> room temperature

SUBSTAGE(3) 15 minutes, room temperature

STAGE(2)

RGT BH 144-55-8 NaHCO₃

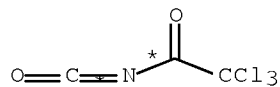
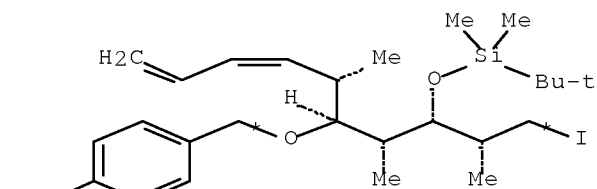
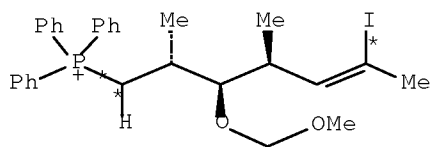
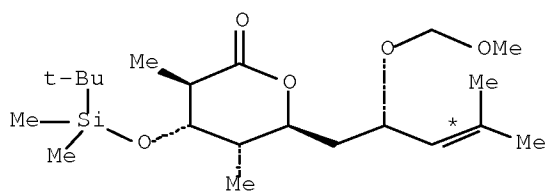
SOL 7732-18-5 Water

CON room temperature

PRO CD 852049-60-6

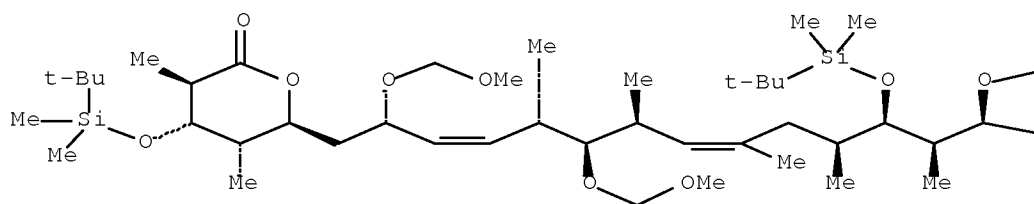
RX(144) OF 178 COMPOSED OF RX(19), RX(20), RX(21), RX(22), RX(23)

RX(144) BZ + BR + AZ + CE ==> CF

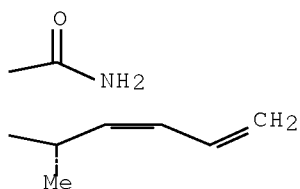


5
STEPS
→

PAGE 1-A



PAGE 1-B



CF
YIELD 92%

RX(19) RCT BZ 852049-62-8

STAGE(1)

RGT AM 7782-44-7 O₂, AN 10028-15-6 Ozone

SOL 75-09-2 CH₂Cl₂

CON -78 deg C

STAGE(2)

RGT BB 603-35-0 PPh₃

CON 1 hour, room temperature

PRO CA 852049-57-1

RX(20) RCT BR 850211-72-2

STAGE(1)

RGT BU 1070-89-9 (Me₃Si)₂N.Na

SOL 109-99-9 THF

CON 1 hour, -78 deg C

STAGE(2)

RCT CA 852049-57-1

SOL 109-99-9 THF

CON SUBSTAGE(1) 2 hours, -78 deg C

SUBSTAGE(2) -78 deg C -> -10 deg C

SUBSTAGE(3) 2 hours, -10 deg C

STAGE(3)

RGT AJ 12125-02-9 NH₄Cl

SOL 7732-18-5 Water, 60-29-7 Et₂O

PRO CB 852049-58-2

RX(21) RCT AZ 850211-69-7

STAGE(1)

RGT BM 750545-03-0 Borate(1-),
1,5-cyclooctanediylhydromethoxy-, (T-4)-, AS 594-19-4
t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> room temperature
SUBSTAGE(3) 1 hour, room temperature

STAGE(2)

RCT CB 852049-58-2
RGT BW 603-32-7 Ph3As, BN 534-17-8 Cs2CO3
CAT 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

PRO CC 852049-59-3

RX(22) RCT CC 852049-59-3

STAGE(1)

RGT BG 84-58-2 DDQ
SOL 7732-18-5 Water, 75-09-2 CH2Cl2
CON SUBSTAGE(1) 30 minutes, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature
SUBSTAGE(3) 15 minutes, room temperature

STAGE(2)

RGT BH 144-55-8 NaHCO3
SOL 7732-18-5 Water
CON room temperature

PRO CD 852049-60-6

RX(23) RCT CD 852049-60-6, CE 3019-71-4

STAGE(1)

SOL 75-09-2 CH2Cl2, 108-88-3 PhMe
CON 30 minutes, room temperature

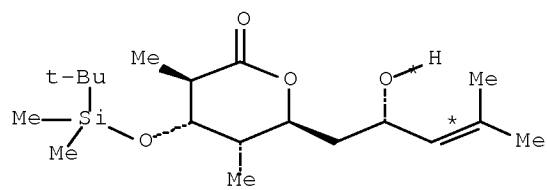
STAGE(2)

RGT CG 1344-28-1 Al2O3
CON 4 hours, room temperature

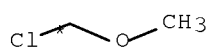
PRO CF 852049-61-7

RX(145) OF 178 COMPOSED OF RX(18), RX(19), RX(20), RX(21), RX(22), RX(23)

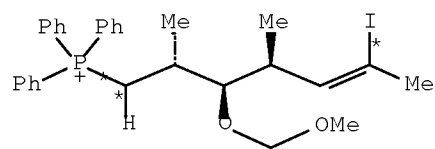
RX(145) BX + BY + ER + AZ + CE ==> CF



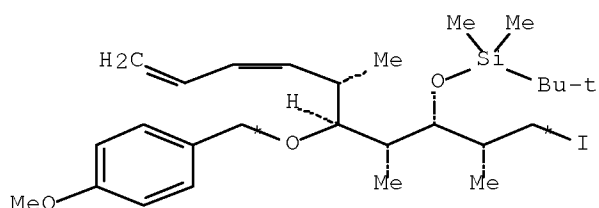
BX



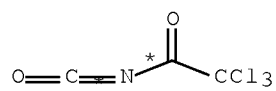
BY



BR



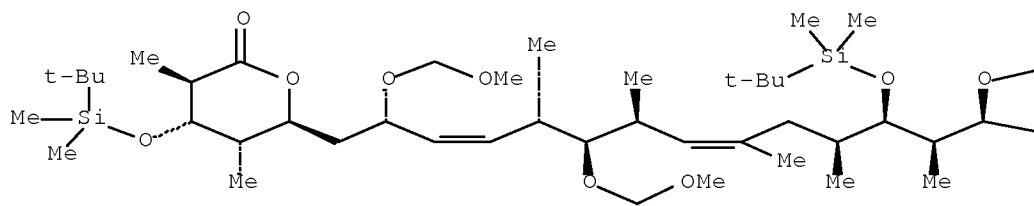
AZ

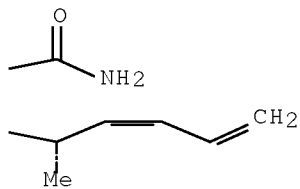


CE

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STEPS
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CF
YIELD 92%

RX(18) RCT BX 256920-77-1, BY 107-30-2

STAGE(1)

RGT H 7087-68-5 EtN(Pr-i)₂
SOL 75-09-2 CH₂Cl₂
CON 12 hours, room temperature

STAGE(2)

RGT BK 7647-14-5 NaCl
SOL 7732-18-5 Water
CON room temperature

PRO BZ 852049-62-8

RX(19) RCT BZ 852049-62-8

STAGE(1)

RGT AM 7782-44-7 O₂, AN 10028-15-6 Ozone
SOL 75-09-2 CH₂Cl₂
CON -78 deg C

STAGE(2)

RGT BB 603-35-0 PPh₃
CON 1 hour, room temperature

PRO CA 852049-57-1

RX(20) RCT BR 850211-72-2

STAGE(1)

RGT BU 1070-89-9 (Me₃Si)₂N.Na
SOL 109-99-9 THF
CON 1 hour, -78 deg C

STAGE(2)

RCT CA 852049-57-1
SOL 109-99-9 THF
CON SUBSTAGE(1) 2 hours, -78 deg C
SUBSTAGE(2) -78 deg C -> -10 deg C
SUBSTAGE(3) 2 hours, -10 deg C

STAGE(3)

RGT AJ 12125-02-9 NH₄Cl
SOL 7732-18-5 Water, 60-29-7 Et₂O

PRO CB 852049-58-2

RX(21) RCT AZ 850211-69-7

STAGE(1)

RGT BM 750545-03-0 Borate(1-),
1,5-cyclooctanediylhydromethoxy-, (T-4)-, AS 594-19-4
t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> room temperature
SUBSTAGE(3) 1 hour, room temperature

STAGE(2)

RCT CB 852049-58-2
RGT BW 603-32-7 Ph3As, BN 534-17-8 Cs2CO3
CAT 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

PRO CC 852049-59-3

RX(22) RCT CC 852049-59-3

STAGE(1)

RGT BG 84-58-2 DDQ
SOL 7732-18-5 Water, 75-09-2 CH2Cl2
CON SUBSTAGE(1) 30 minutes, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature
SUBSTAGE(3) 15 minutes, room temperature

STAGE(2)

RGT BH 144-55-8 NaHCO3
SOL 7732-18-5 Water
CON room temperature

PRO CD 852049-60-6

RX(23) RCT CD 852049-60-6, CE 3019-71-4

STAGE(1)

SOL 75-09-2 CH2Cl2, 108-88-3 PhMe
CON 30 minutes, room temperature

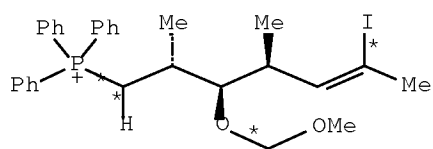
STAGE(2)

RGT CG 1344-28-1 Al2O3
CON 4 hours, room temperature

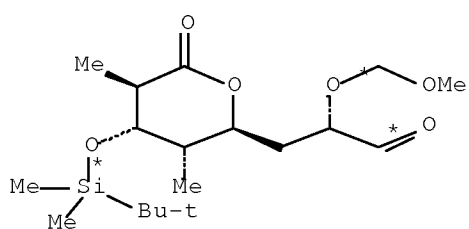
PRO CF 852049-61-7

RX(146) OF 178 COMPOSED OF RX(20), RX(21), RX(22), RX(23), RX(24)

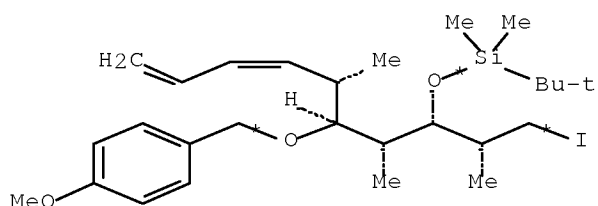
RX(146) BR + CA + AZ + CE ==> CI



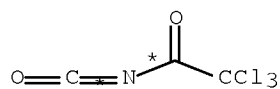
BR



CA

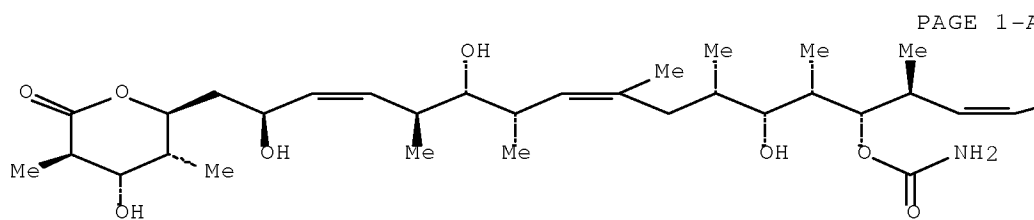


AZ



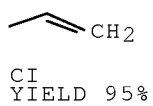
CE

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STEPS
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PAGE 1-B



CI
YIELD 95%

RX(20) RCT BR 850211-72-2

STAGE(1)

RGT BU 1070-89-9 (Me3Si)2N.Na
SOL 109-99-9 THF
CON 1 hour, -78 deg C

STAGE(2)

RCT CA 852049-57-1
SOL 109-99-9 THF
CON SUBSTAGE(1) 2 hours, -78 deg C
SUBSTAGE(2) -78 deg C -> -10 deg C
SUBSTAGE(3) 2 hours, -10 deg C

STAGE(3)

RGT AJ 12125-02-9 NH4Cl
SOL 7732-18-5 Water, 60-29-7 Et2O

PRO CB 852049-58-2

RX(21) RCT AZ 850211-69-7

STAGE(1)

RGT BM 750545-03-0 Borate(1-),
1,5-cyclooctanediylhydromethoxy-, (T-4)-, AS 594-19-4
t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> room temperature
SUBSTAGE(3) 1 hour, room temperature

STAGE(2)

RCT CB 852049-58-2
RGT BW 603-32-7 Ph3As, BN 534-17-8 Cs2CO3
CAT 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

PRO CC 852049-59-3

RX(22) RCT CC 852049-59-3

STAGE(1)

RGT BG 84-58-2 DDQ
SOL 7732-18-5 Water, 75-09-2 CH2Cl2
CON SUBSTAGE(1) 30 minutes, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature
SUBSTAGE(3) 15 minutes, room temperature

STAGE(2)

RGT BH 144-55-8 NaHCO3
SOL 7732-18-5 Water
CON room temperature

PRO CD 852049-60-6

RX(23) RCT CD 852049-60-6, CE 3019-71-4

STAGE(1)

SOL 75-09-2 CH₂Cl₂, 108-88-3 PhMe
CON 30 minutes, room temperature

STAGE(2)

RGT CG 1344-28-1 Al₂O₃
CON 4 hours, room temperature

PRO CF 852049-61-7

RX(24) RCT CF 852049-61-7

STAGE(1)

RGT CJ 7647-01-0 HCl
SOL 7732-18-5 Water, 67-56-1 MeOH
CON SUBSTAGE(1) 15 minutes, room temperature
SUBSTAGE(2) 6 hours, room temperature

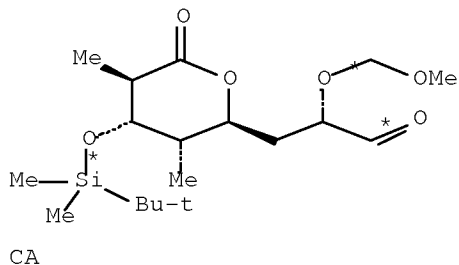
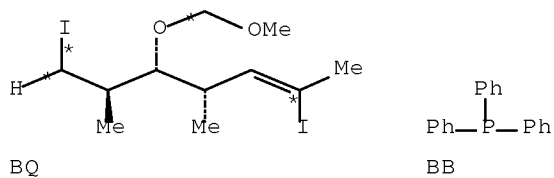
STAGE(2)

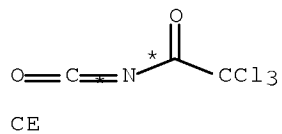
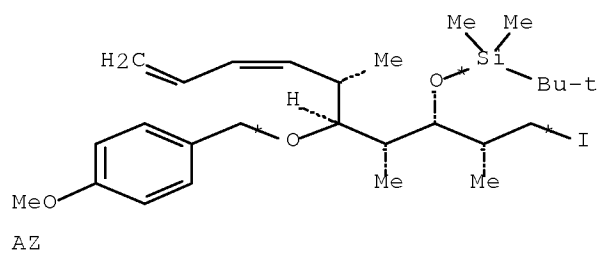
RGT BH 144-55-8 NaHCO₃
CON room temperature

PRO CI 127943-53-7

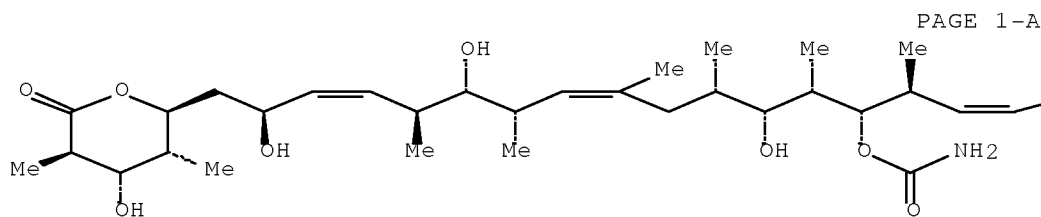
RX(147) OF 178 COMPOSED OF RX(15), RX(20), RX(21), RX(22), RX(23), RX(24)

RX(147) BQ + BB + CA + AZ + CE ==> CI

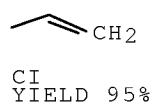




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STEPS
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PAGE 1-B



RX(15) RCT BQ 850211-71-1, BB 603-35-0
 PRO BR 850211-72-2
 CON SUBSTAGE(1) room temperature -> 95 deg C
 SUBSTAGE(2) 18 hours, 95 deg C

RX(20) RCT BR 850211-72-2
 STAGE(1)
 RGT BU 1070-89-9 (Me3Si)2N.Na
 SOL 109-99-9 THF
 CON 1 hour, -78 deg C

STAGE(2)

RCT CA 852049-57-1
SOL 109-99-9 THF
CON SUBSTAGE(1) 2 hours, -78 deg C
SUBSTAGE(2) -78 deg C -> -10 deg C
SUBSTAGE(3) 2 hours, -10 deg C

STAGE(3)
RGT AJ 12125-02-9 NH4Cl
SOL 7732-18-5 Water, 60-29-7 Et2O

PRO CB 852049-58-2

RX(21) RCT AZ 850211-69-7

STAGE(1)
RGT BM 750545-03-0 Borate(1-),
1,5-cyclooctanediylhydromethoxy-, (T-4)-, AS 594-19-4
t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> room temperature
SUBSTAGE(3) 1 hour, room temperature

STAGE(2)
RCT CB 852049-58-2
RGT BW 603-32-7 Ph3As, BN 534-17-8 Cs2CO3
CAT 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

PRO CC 852049-59-3

RX(22) RCT CC 852049-59-3

STAGE(1)
RGT BG 84-58-2 DDQ
SOL 7732-18-5 Water, 75-09-2 CH2Cl2
CON SUBSTAGE(1) 30 minutes, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature
SUBSTAGE(3) 15 minutes, room temperature

STAGE(2)
RGT BH 144-55-8 NaHCO3
SOL 7732-18-5 Water
CON room temperature

PRO CD 852049-60-6

RX(23) RCT CD 852049-60-6, CE 3019-71-4

STAGE(1)
SOL 75-09-2 CH2Cl2, 108-88-3 PhMe
CON 30 minutes, room temperature

STAGE(2)
RGT CG 1344-28-1 Al2O3
CON 4 hours, room temperature

PRO CF 852049-61-7

RX(24) RCT CF 852049-61-7

STAGE(1)

RGT CJ 7647-01-0 HCl

SOL 7732-18-5 Water, 67-56-1 MeOH

CON SUBSTAGE(1) 15 minutes, room temperature

SUBSTAGE(2) 6 hours, room temperature

STAGE(2)

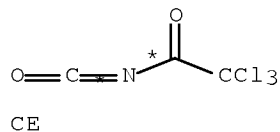
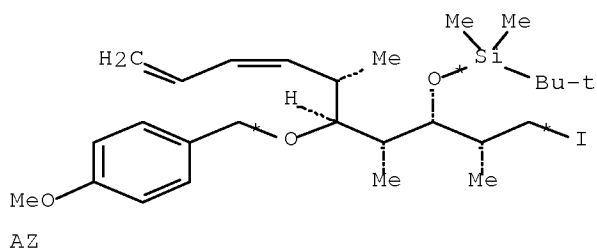
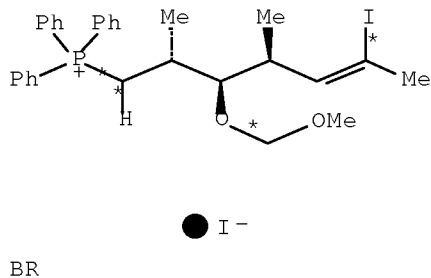
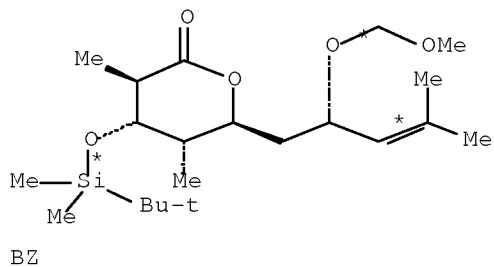
RGT BH 144-55-8 NaHCO3

CON room temperature

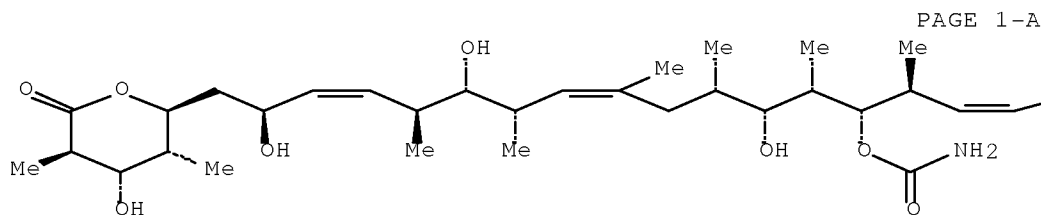
PRO CI 127943-53-7

RX(148) OF 178 COMPOSED OF RX(19), RX(20), RX(21), RX(22), RX(23), RX(24)

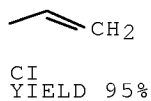
RX(148) BZ + BR + AZ + CE ==> CI



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STEPS
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RX(19) RCT BZ 852049-62-8

STAGE(1)

RGT AM 7782-44-7 O₂, AN 10028-15-6 Ozone

SOL 75-09-2 CH₂Cl₂

CON -78 deg C

STAGE(2)

RGT BB 603-35-0 PPh₃

CON 1 hour, room temperature

PRO CA 852049-57-1

RX(20) RCT BR 850211-72-2

STAGE(1)

RGT BU 1070-89-9 (Me₃Si)₂N.Na

SOL 109-99-9 THF

CON 1 hour, -78 deg C

STAGE(2)

RCT CA 852049-57-1

SOL 109-99-9 THF

CON SUBSTAGE(1) 2 hours, -78 deg C

SUBSTAGE(2) -78 deg C -> -10 deg C

SUBSTAGE(3) 2 hours, -10 deg C

STAGE(3)

RGT AJ 12125-02-9 NH₄Cl

SOL 7732-18-5 Water, 60-29-7 Et₂O

PRO CB 852049-58-2

RX(21) RCT AZ 850211-69-7

STAGE(1)

RGT BM 750545-03-0 Borate(1-),
1,5-cyclooctanediylhydromethoxy-, (T-4)-, AS 594-19-4
t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> room temperature
SUBSTAGE(3) 1 hour, room temperature

STAGE(2)

RCT CB 852049-58-2
RGT BW 603-32-7 Ph3As, BN 534-17-8 Cs2CO3
CAT 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

PRO CC 852049-59-3

RX(22) RCT CC 852049-59-3

STAGE(1)

RGT BG 84-58-2 DDQ
SOL 7732-18-5 Water, 75-09-2 CH2Cl2
CON SUBSTAGE(1) 30 minutes, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature
SUBSTAGE(3) 15 minutes, room temperature

STAGE(2)

RGT BH 144-55-8 NaHCO3
SOL 7732-18-5 Water
CON room temperature

PRO CD 852049-60-6

RX(23) RCT CD 852049-60-6, CE 3019-71-4

STAGE(1)

SOL 75-09-2 CH2Cl2, 108-88-3 PhMe
CON 30 minutes, room temperature

STAGE(2)

RGT CG 1344-28-1 Al2O3
CON 4 hours, room temperature

PRO CF 852049-61-7

RX(24) RCT CF 852049-61-7

STAGE(1)

RGT CJ 7647-01-0 HCl
SOL 7732-18-5 Water, 67-56-1 MeOH
CON SUBSTAGE(1) 15 minutes, room temperature
SUBSTAGE(2) 6 hours, room temperature

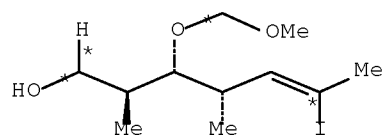
STAGE(2)

RGT BH 144-55-8 NaHCO3
CON room temperature

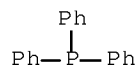
PRO CI 127943--53--7

RX(149) OF 178 COMPOSED OF RX(14), RX(15), RX(20), RX(21), RX(22), RX(23),
RX(24)

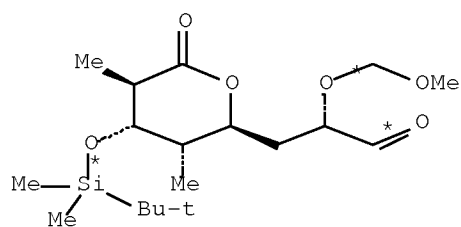
RX(149) EF + BB + CA + AZ + CE ==> CI



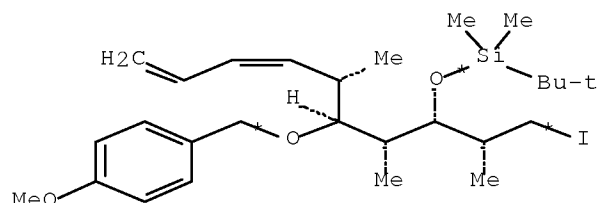
BF



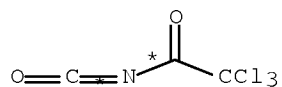
BB



CA

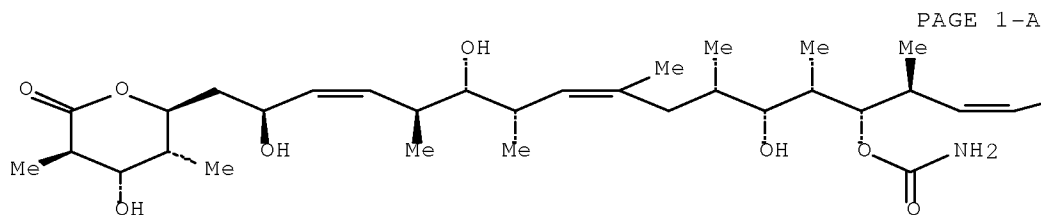


AZ

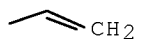


CE

7
STEPS
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PAGE 1-B



CI
YIELD 95%

RX(14) RCT BF 850211-70-0

STAGE(1)

RGT BA 7553-56-2 I2, BB 603-35-0 PPh3, BC 288-32-4 1H-Imidazole
SOL 60-29-7 Et2O, 71-43-2 Benzene
CON SUBSTAGE(1) 0 deg C -> room temperature
SUBSTAGE(2) 12 hours, room temperature

STAGE(2)

RGT BH 144-55-8 NaHCO3
SOL 7732-18-5 Water
CON room temperature

PRO BQ 850211-71-1

RX(15) RCT BQ 850211-71-1, BB 603-35-0
PRO BR 850211-72-2
CON SUBSTAGE(1) room temperature -> 95 deg C
SUBSTAGE(2) 18 hours, 95 deg C

RX(20) RCT BR 850211-72-2

STAGE(1)

RGT BU 1070-89-9 (Me3Si)2N.Na
SOL 109-99-9 THF
CON 1 hour, -78 deg C

STAGE(2)

RCT CA 852049-57-1
SOL 109-99-9 THF
CON SUBSTAGE(1) 2 hours, -78 deg C
SUBSTAGE(2) -78 deg C -> -10 deg C
SUBSTAGE(3) 2 hours, -10 deg C

STAGE(3)

RGT AJ 12125-02-9 NH4Cl

SOL 7732-18-5 Water, 60-29-7 Et2O

PRO CB 852049-58-2

RX(21) RCT AZ 850211-69-7

STAGE(1)

RGT BM 750545-03-0 Borate(1-),
1,5-cyclooctanediylhydromethoxy-, (T-4)-, AS 594-19-4
t-BuLi

SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane

CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> room temperature
SUBSTAGE(3) 1 hour, room temperature

STAGE(2)

RCT CB 852049-58-2

RGT BW 603-32-7 Ph3As, BN 534-17-8 Cs2CO3

CAT 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-

SOL 7732-18-5 Water, 68-12-2 DMF

CON 20 hours, room temperature

PRO CC 852049-59-3

RX(22) RCT CC 852049-59-3

STAGE(1)

RGT BG 84-58-2 DDQ

SOL 7732-18-5 Water, 75-09-2 CH2Cl2

CON SUBSTAGE(1) 30 minutes, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature
SUBSTAGE(3) 15 minutes, room temperature

STAGE(2)

RGT BH 144-55-8 NaHCO3

SOL 7732-18-5 Water

CON room temperature

PRO CD 852049-60-6

RX(23) RCT CD 852049-60-6, CE 3019-71-4

STAGE(1)

SOL 75-09-2 CH2Cl2, 108-88-3 PhMe

CON 30 minutes, room temperature

STAGE(2)

RGT CG 1344-28-1 Al2O3

CON 4 hours, room temperature

PRO CF 852049-61-7

RX(24) RCT CF 852049-61-7

STAGE(1)

RGT CJ 7647-01-0 HCl

SOL 7732-18-5 Water, 67-56-1 MeOH

CON SUBSTAGE(1) 15 minutes, room temperature
 SUBSTAGE(2) 6 hours, room temperature

STAGE(2)

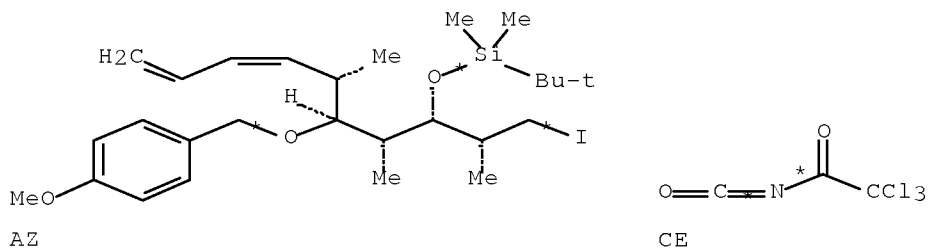
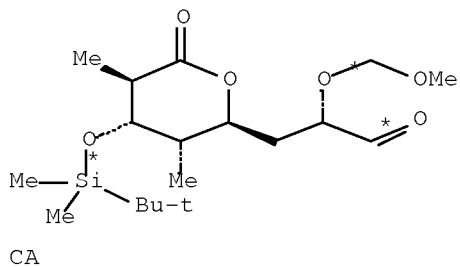
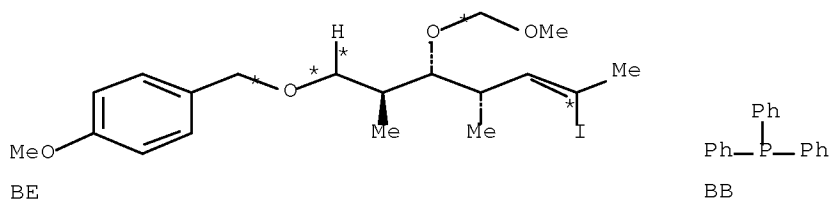
RGT BH 144-55-8 NaHCO3

CON room temperature

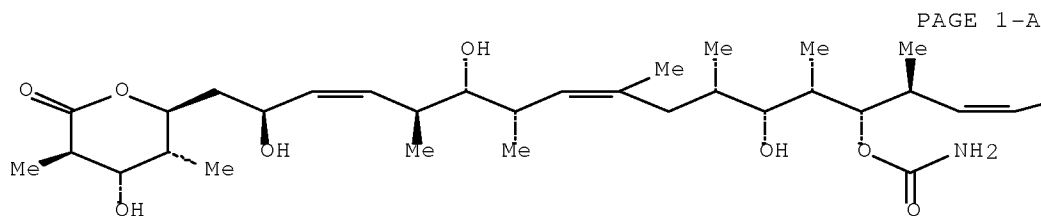
PRO CI 127943-53-7

RX(150) OF 178 COMPOSED OF RX(11), RX(14), RX(15), RX(20), RX(21), RX(22),
 RX(23), RX(24)

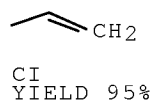
RX(150) BE + BB + CA + AZ + CE ==> CI



8
STEPS
→



PAGE 1-B



RX(11) RCT BE 633294-02-7

STAGE(1)

RGT BG 84-58-2 DDQ
SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
CON 2 hours, 0 deg C

STAGE(2)

RGT BH 144-55-8 NaHCO₃
SOL 7732-18-5 Water

PRO BF 850211-70-0

RX(14) RCT BF 850211-70-0

STAGE(1)

RGT BA 7553-56-2 I₂, BB 603-35-0 PPh₃, BC 288-32-4 1H-Imidazole
SOL 60-29-7 Et₂O, 71-43-2 Benzene
CON SUBSTAGE(1) 0 deg C -> room temperature
SUBSTAGE(2) 12 hours, room temperature

STAGE(2)

RGT BH 144-55-8 NaHCO₃
SOL 7732-18-5 Water
CON room temperature

PRO BQ 850211-71-1

RX(15) RCT BQ 850211-71-1, BB 603-35-0
 PRO BR 850211-72-2
 CON SUBSTAGE(1) room temperature -> 95 deg C
 SUBSTAGE(2) 18 hours, 95 deg C

RX(20) RCT BR 850211-72-2

STAGE(1)
 RGT BU 1070-89-9 (Me3Si)2N.Na
 SOL 109-99-9 THF
 CON 1 hour, -78 deg C

STAGE(2)
 RCT CA 852049-57-1
 SOL 109-99-9 THF
 CON SUBSTAGE(1) 2 hours, -78 deg C
 SUBSTAGE(2) -78 deg C -> -10 deg C
 SUBSTAGE(3) 2 hours, -10 deg C

STAGE(3)
 RGT AJ 12125-02-9 NH4Cl
 SOL 7732-18-5 Water, 60-29-7 Et2O

PRO CB 852049-58-2

RX(21) RCT AZ 850211-69-7

STAGE(1)
 RGT BM 750545-03-0 Borate(1-),
 1,5-cyclooctanediylhydromethoxy-, (T-4)-, AS 594-19-4
 t-BuLi
 SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
 Pentane
 CON SUBSTAGE(1) -78 deg C
 SUBSTAGE(2) -78 deg C -> room temperature
 SUBSTAGE(3) 1 hour, room temperature

STAGE(2)
 RCT CB 852049-58-2
 RGT BW 603-32-7 Ph3As, BN 534-17-8 Cs2CO3
 CAT 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

PRO CC 852049-59-3

RX(22) RCT CC 852049-59-3

STAGE(1)
 RGT BG 84-58-2 DDQ
 SOL 7732-18-5 Water, 75-09-2 CH2Cl2
 CON SUBSTAGE(1) 30 minutes, 0 deg C
 SUBSTAGE(2) 0 deg C -> room temperature
 SUBSTAGE(3) 15 minutes, room temperature

STAGE(2)
 RGT BH 144-55-8 NaHCO3
 SOL 7732-18-5 Water

CON room temperature

PRO CD 852049-60-6

RX(23) RCT CD 852049-60-6, CE 3019-71-4

STAGE(1)

SOL 75-09-2 CH₂Cl₂, 108-88-3 PhMe

CON 30 minutes, room temperature

STAGE(2)

RGT CG 1344-28-1 Al₂O₃

CON 4 hours, room temperature

PRO CF 852049-61-7

RX(24) RCT CF 852049-61-7

STAGE(1)

RGT CJ 7647-01-0 HCl

SOL 7732-18-5 Water, 67-56-1 MeOH

CON SUBSTAGE(1) 15 minutes, room temperature

SUBSTAGE(2) 6 hours, room temperature

STAGE(2)

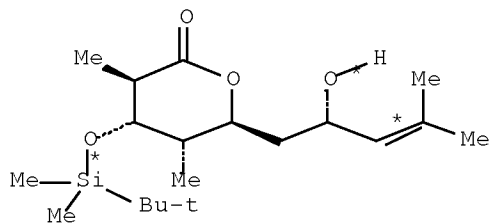
RGT BH 144-55-8 NaHCO₃

CON room temperature

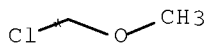
PRO CI 127943-53-7

RX(151) OF 178 COMPOSED OF RX(18), RX(19), RX(20), RX(21), RX(22), RX(23),
RX(24)

RX(151) BX + BY + BR + AZ + CE ==> CI



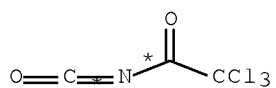
BX



BY

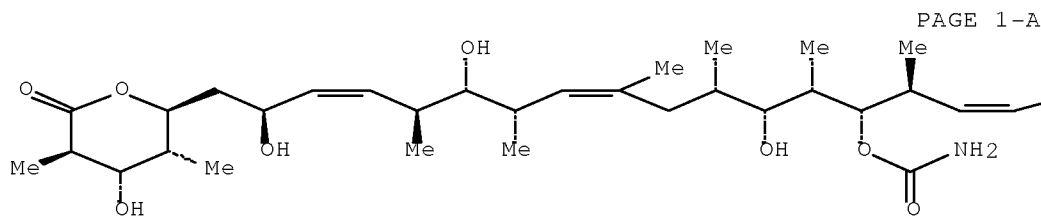


AZ



CE

7
STEPS
→



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PAGE 1-B



CI
YIELD 95%

RX(18) RCT BX 256920-77-1, BY 107-30-2

STAGE (1)

RGT H 7087-68-5 EtN(Pr-i)2

SOL 75-09-2 CH2C12

CON 12 hours, room temperature

STAGE (2)

RGT BK 7647-14-5 NaCl

SOL 7732-18-5 Water
 CON room temperature

PRO BZ 852049-62-8

RX(19) RCT BZ 852049-62-8

STAGE(1)
 RGT AM 7782-44-7 O2, AN 10028-15-6 Ozone
 SOL 75-09-2 CH2Cl2
 CON -78 deg C

STAGE(2)
 RGT BB 603-35-0 PPh3
 CON 1 hour, room temperature

PRO CA 852049-57-1

RX(20) RCT BR 850211-72-2

STAGE(1)
 RGT BU 1070-89-9 (Me3Si)2N.Na
 SOL 109-99-9 THF
 CON 1 hour, -78 deg C

STAGE(2)
 RCT CA 852049-57-1
 SOL 109-99-9 THF
 CON SUBSTAGE(1) 2 hours, -78 deg C
 SUBSTAGE(2) -78 deg C -> -10 deg C
 SUBSTAGE(3) 2 hours, -10 deg C

STAGE(3)
 RGT AJ 12125-02-9 NH4Cl
 SOL 7732-18-5 Water, 60-29-7 Et2O

PRO CB 852049-58-2

RX(21) RCT AZ 850211-69-7

STAGE(1)
 RGT BM 750545-03-0 Borate(1-),
 1,5-cyclooctanediyldromethoxy-, (T-4)-, AS 594-19-4
 t-BuLi
 SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
 Pentane
 CON SUBSTAGE(1) -78 deg C
 SUBSTAGE(2) -78 deg C -> room temperature
 SUBSTAGE(3) 1 hour, room temperature

STAGE(2)
 RCT CB 852049-58-2
 RGT BW 603-32-7 Ph3As, BN 534-17-8 Cs2CO3
 CAT 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

PRO CC 852049-59-3

RX(22) RCT CC 852049-59-3

STAGE(1)

RGT BG 84-58-2 DDQ
SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
CON SUBSTAGE(1) 30 minutes, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature
SUBSTAGE(3) 15 minutes, room temperature

STAGE(2)

RGT BH 144-55-8 NaHCO₃
SOL 7732-18-5 Water
CON room temperature

PRO CD 852049-60-6

RX(23) RCT CD 852049-60-6, CE 3019-71-4

STAGE(1)

SOL 75-09-2 CH₂Cl₂, 108-88-3 PhMe
CON 30 minutes, room temperature

STAGE(2)

RGT CG 1344-28-1 Al₂O₃
CON 4 hours, room temperature

PRO CF 852049-61-7

RX(24) RCT CF 852049-61-7

STAGE(1)

RGT CJ 7647-01-0 HCl
SOL 7732-18-5 Water, 67-56-1 MeOH
CON SUBSTAGE(1) 15 minutes, room temperature
SUBSTAGE(2) 6 hours, room temperature

STAGE(2)

RGT BH 144-55-8 NaHCO₃
CON room temperature

PRO CI 127943-53-7

L3 ANSWER 6 OF 9 CASREACT COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 142:481862 CASREACT Full-text
TITLE: Crotylsilane Reagents in the Synthesis of Complex
Polyketide Natural Products: Total Synthesis of
(+)-Discodermolide
AUTHOR(S): Arefolov, Alexander; Panek, James S.
CORPORATE SOURCE: Department of Chemistry and Center for Chemical
Methodology and Library Development, Metcalf Center
for Science and Engineering, Boston University,
Boston, 02215, USA
SOURCE: Journal of the American Chemical Society (2005),
127(15), 5596-5603
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

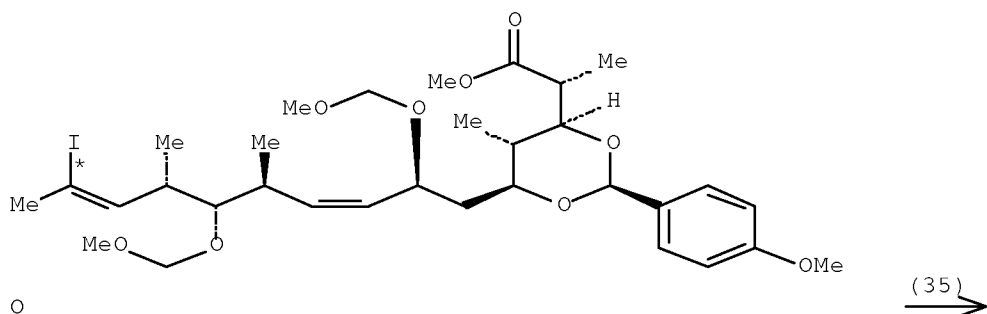
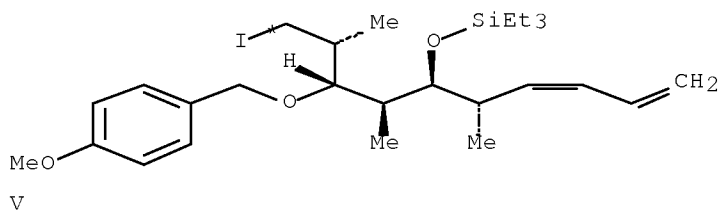
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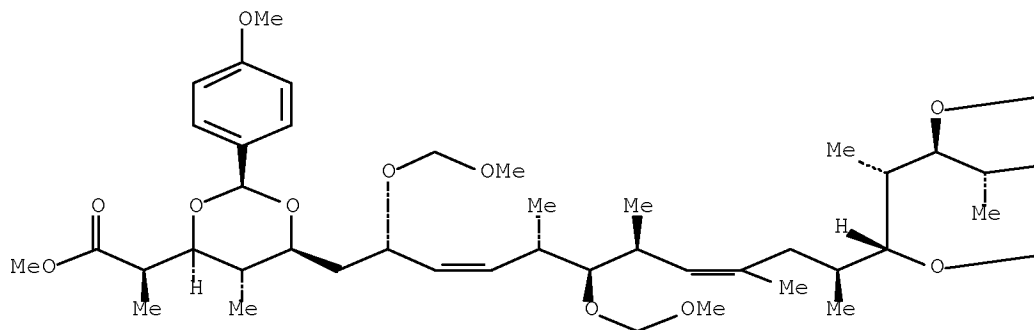
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB An efficient, highly convergent stereocontrolled synthesis of (+)-discodermolide (I) has been achieved with 2.1% overall yield (27 steps longest linear sequence). The absolute stereochem. of the C1-C6 (II; PMP = C6H4OMe-4), C7-C14 (III; TBS = SiMe2CMe3), and C15-C24 (IV; PMB = CH2C6H4OMe-4) subunits was introduced using asym. crotylation methodol. Key elements of the synthesis include the use of hydrozirconation-cross-coupling methodol. for the construction of C13-C14 (Z)-olefin, acetate aldol reaction to construct the C6-C7 bond and install the C7 stereocenter with high levels of 1,5-anti stereoinduction, and the use of palladium-mediated sp2-sp3 cross-coupling reaction to join the advanced fragments, which assembled the carbon framework of discodermolide.

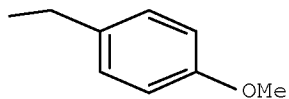
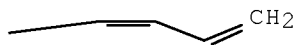
REFERENCE COUNT: 107 THERE ARE 107 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

RX(35) OF 576 ...V + O ==> DJ...





— SiEt₃



DJ
YIELD 82%

RX(35) RCT V 216669--69--1

STAGE(1)

SOL 60-29-7 Et₂O

CON room temperature -> -78 deg C

STAGE(2)

RGT DK 594-19-4 t-BuLi

SOL 109-66-0 Pentane

CON 30 minutes, -78 deg C

STAGE(3)

RGT BO 7646-85-7 ZnCl₂

SOL 109-99-9 THF

CON SUBSTAGE(1) 5 minutes, -78 deg C

SUBSTAGE(2) 30 minutes, -78 deg C -> 0 deg C

STAGE(4)

RCT O 851889-66-2

CAT 14221-01-3 Pd(PPh₃)₄

SOL 109-99-9 THF

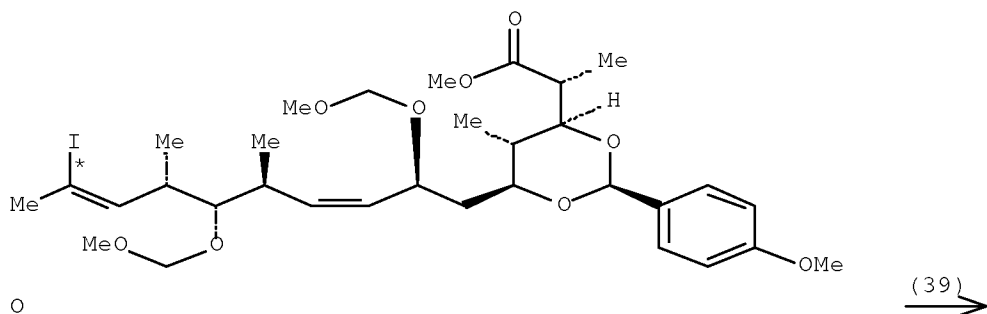
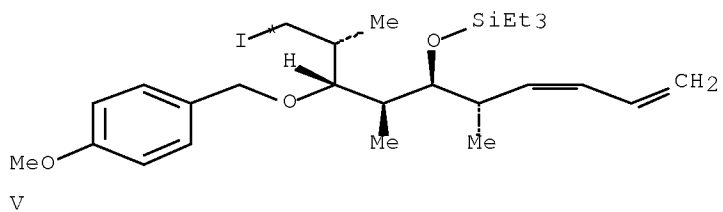
CON SUBSTAGE(1) 1 hour, 0 deg C
 SUBSTAGE(2) 0 deg C -> room temperature
 SUBSTAGE(3) 6 hours, room temperature

STAGE(5)

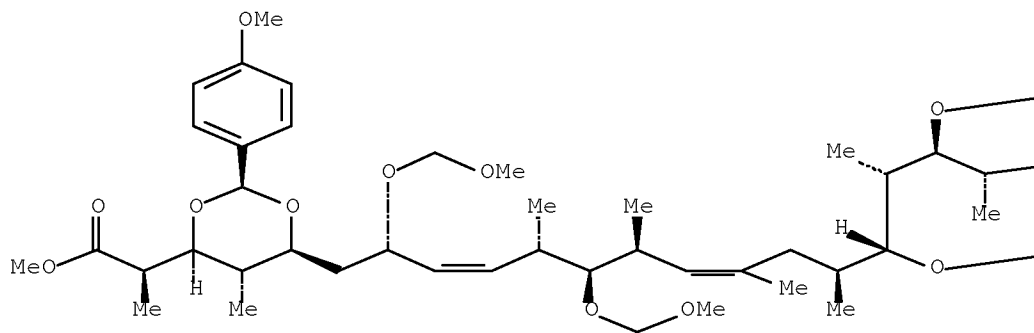
SOL 7732-18-5 Water
 CON room temperature

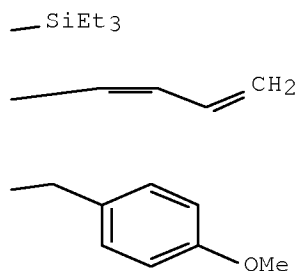
PRO DJ 851889-85-5
 NTE last stage quench

RX(39) OF 576 V + O ==> DJ



PAGE 1-A





DJ
YIELD 82%

RX(39) RCT V 216669-69-1

STAGE(1)

SOL 60-29-7 Et2O

CON room temperature -> -78 deg C

STAGE(2)

RGT DK 594-19-4 t-BuLi

SOL 109-66-0 Pentane

CON 3 minutes, -78 deg C

STAGE(3)

RGT DO 38050-71-4 9-BBN-OMe

SOL 110-54-3 Hexane

CON -78 deg C

STAGE(4)

SOL 109-99-9 THF

CON SUBSTAGE(1) 10 minutes, -78 deg C

SUBSTAGE(2) 1 hour, -78 deg C -> room temperature

STAGE(5)

SOL 7732-18-5 Water

CON room temperature

STAGE(6)

RGT DP 20398-06-5 Tl(OEt)

CON room temperature

STAGE(7)

RCT O 851889-66-2

SOL 68-12-2 DMF

CON room temperature

STAGE(8)

CAT 72287-26-4 Palladium,

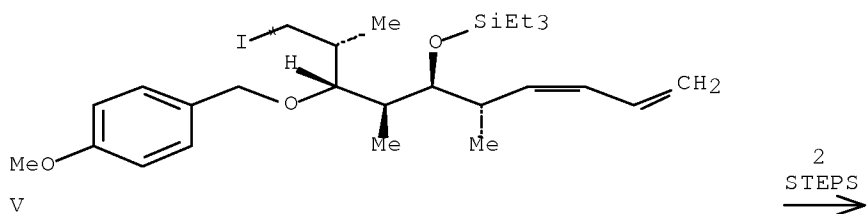
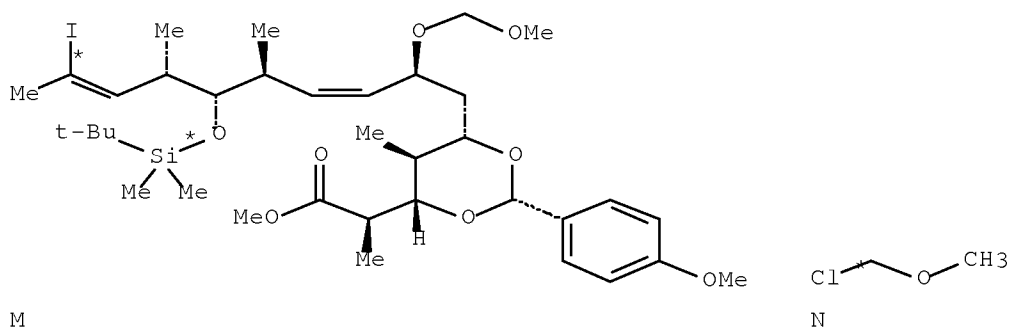
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,

(SP-4-2)-
 CON 14 hours, room temperature

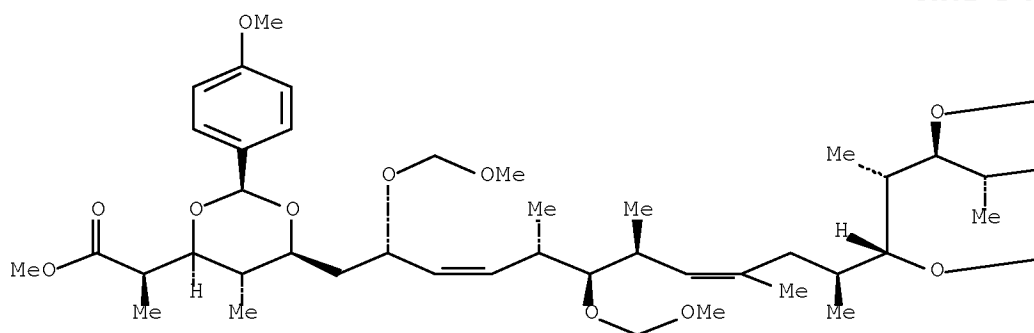
STAGE(9)
 SOL 7732-18-5 Water
 CON room temperature

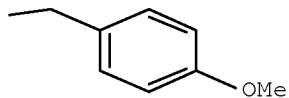
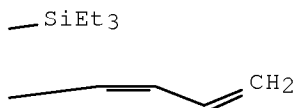
PRO DJ 851889-85-5
 NTE fifth stage quench

RX(41) OF 576 COMPOSED OF RX(3), RX(35)
 RX(41) M + N + V ==> DJ



PAGE 1-A





DJ
YIELD 82%

RX(3) RCT M 851889-82-2

STAGE(1)

SOL 109-99-9 THF
CON room temperature

STAGE(2)

RGT P 64-19-7 AcOH, Q 429-41-4 Bu4N.F
SOL 109-99-9 THF
CON 36 hours, room temperature

STAGE(3)

SOL 7732-18-5 Water
CON room temperature, pH 7

STAGE(4)

RGT R 7087-68-5 EtN(Pr-i)2
SOL 56-23-5 CCl4
CON room temperature -> 0 deg C

STAGE(5)

CAT 1122-58-3 4-DMAP
CON 0 deg C

STAGE(6)

RCT N 107-30-2
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 8 hours, 0 deg C -> room temperature

STAGE(7)

RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water

PRO O 851889-66-2

NTE third stage quench

RX(35) RCT V 216669--69--1

STAGE(1)

SOL 60-29-7 Et2O

CON room temperature -> -78 deg C

STAGE(2)

RGT DK 594-19-4 t-BuLi

SOL 109-66-0 Pentane

CON 30 minutes, -78 deg C

STAGE(3)

RGT BO 7646-85-7 ZnCl2

SOL 109-99-9 THF

CON SUBSTAGE(1) 5 minutes, -78 deg C

SUBSTAGE(2) 30 minutes, -78 deg C -> 0 deg C

STAGE(4)

RCT O 851889-66-2

CAT 14221-01-3 Pd(PPh3)4

SOL 109-99-9 THF

CON SUBSTAGE(1) 1 hour, 0 deg C

SUBSTAGE(2) 0 deg C -> room temperature

SUBSTAGE(3) 6 hours, room temperature

STAGE(5)

SOL 7732-18-5 Water

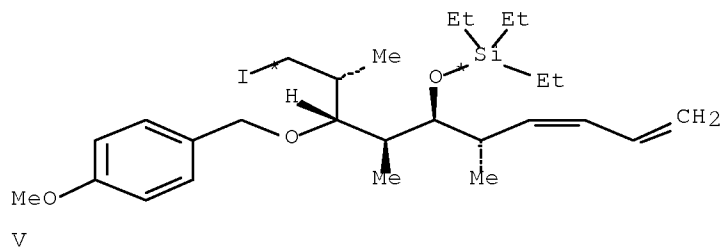
CON room temperature

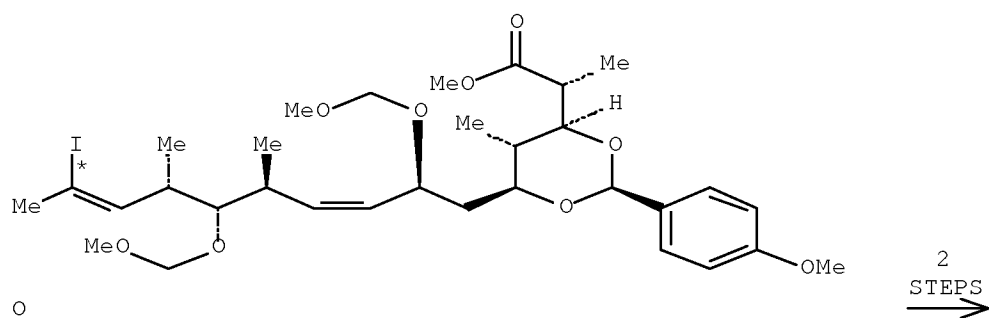
PRO DJ 851889--85--5

NTE last stage quench

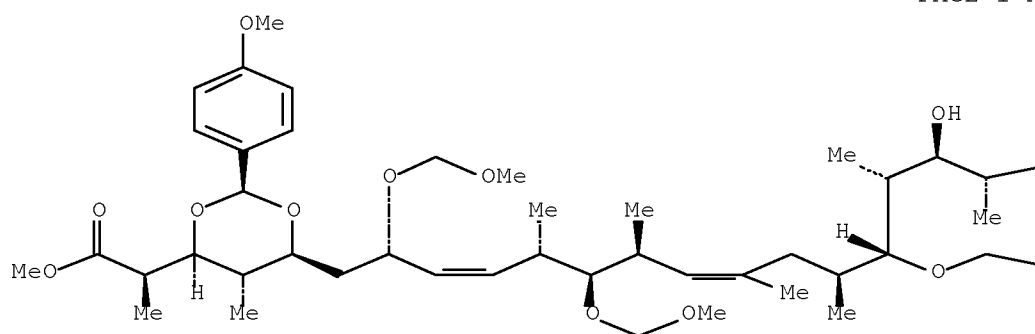
RX(75) OF 576 COMPOSED OF RX(35), RX(36)

RX(75) V + Q ==> G

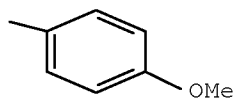




PAGE 1-A



PAGE 1-B



G
YIELD 77%

RX(35) RCT V 216669-69-1

STAGE(1)

SOL 60-29-7 Et2O

CON room temperature -> -78 deg C

STAGE(2)
RGT DK 594-19-4 t-BuLi
SOL 109-66-0 Pentane
CON 30 minutes, -78 deg C

STAGE(3)
RGT BO 7646-85-7 ZnCl2
SOL 109-99-9 THF
CON SUBSTAGE(1) 5 minutes, -78 deg C
SUBSTAGE(2) 30 minutes, -78 deg C -> 0 deg C

STAGE(4)
RCT O ~~851889-56-2~~
CAT 14221-01-3 Pd(PPh3)4
SOL 109-99-9 THF
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature
SUBSTAGE(3) 6 hours, room temperature

STAGE(5)
SOL 7732-18-5 Water
CON room temperature

PRO DJ 851889-85-5
NTE last stage quench

RX(36) RCT DJ 851889-85-5

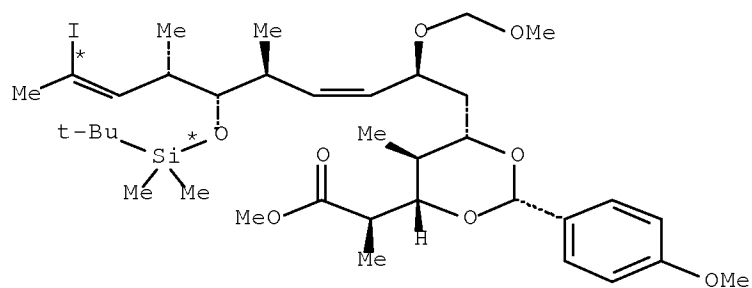
STAGE(1)
SOL 67-56-1 MeOH
CON room temperature -> 0 deg C

STAGE(2)
CAT 104-15-4 TsOH
CON 1 hour, 0 deg C

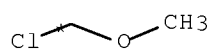
STAGE(3)
RGT AR 121-44-8 Et3N
CON 0 deg C

PRO G ~~851889-86-6~~
NTE last stage quench

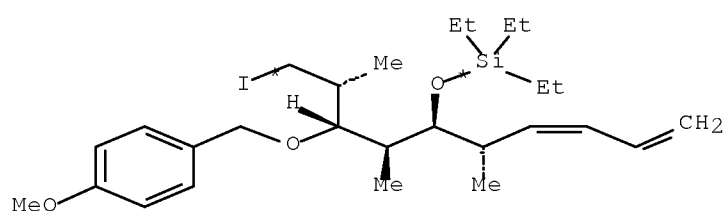
RX(81) OF 576 COMPOSED OF RX(3), RX(35), RX(36)
RX(81) M + N + V ==> G



M



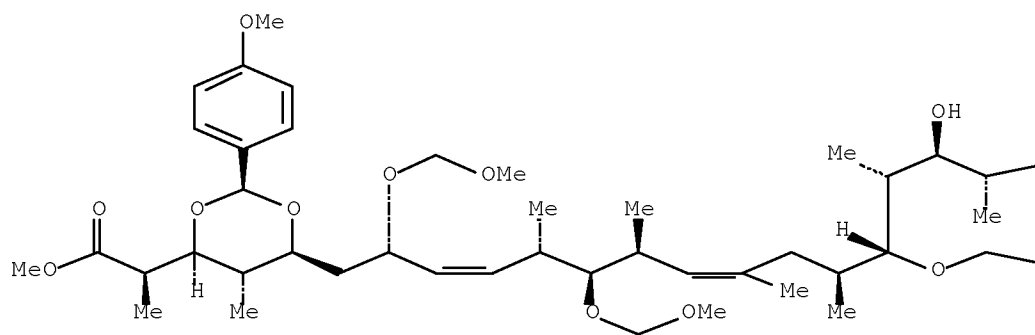
N

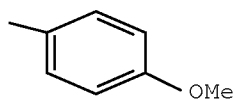
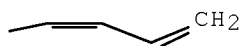


V

3
STEPS
→

PAGE 1-A





^G
YIELD 77%

RX(3) RCT M 851889-82-2

STAGE(1)

SOL 109-99-9 THF
CON room temperature

STAGE(2)

RGT P 64-19-7 AcOH, Q 429-41-4 Bu4N.F
SOL 109-99-9 THF
CON 36 hours, room temperature

STAGE(3)

SOL 7732-18-5 Water
CON room temperature, pH 7

STAGE(4)

RGT R 7087-68-5 EtN(Pr-i)₂
SOL 56-23-5 CCl₄
CON room temperature -> 0 deg C

STAGE(5)

CAT 1122-58-3 4-DMAP
CON 0 deg C

STAGE(6)

RCT N 107-30-2
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 8 hours, 0 deg C -> room temperature

STAGE(7)

RGT D 144-55-8 NaHCO₃
SOL 7732-18-5 Water

PRO O 851889-66-2

NTE third stage quench

RX(35) RCT V 216669-69-1

STAGE(1)

SOL 60-29-7 Et₂O

CON room temperature -> -78 deg C

STAGE(2)

RGT DK 594-19-4 t-BuLi

SOL 109-66-0 Pentane

CON 30 minutes, -78 deg C

STAGE(3)

RGT BO 7646-85-7 ZnCl2

SOL 109-99-9 THF

CON SUBSTAGE(1) 5 minutes, -78 deg C

SUBSTAGE(2) 30 minutes, -78 deg C -> 0 deg C

STAGE(4)

RCT O 851889-66-2

CAT 14221-01-3 Pd(PPh3)4

SOL 109-99-9 THF

CON SUBSTAGE(1) 1 hour, 0 deg C

SUBSTAGE(2) 0 deg C -> room temperature

SUBSTAGE(3) 6 hours, room temperature

STAGE(5)

SOL 7732-18-5 Water

CON room temperature

PRO DJ 851889-85-5

NTE last stage quench

RX(36) RCT DJ 851889-85-5

STAGE(1)

SOL 67-56-1 MeOH

CON room temperature -> 0 deg C

STAGE(2)

CAT 104-15-4 TsOH

CON 1 hour, 0 deg C

STAGE(3)

RGT AR 121-44-8 Et3N

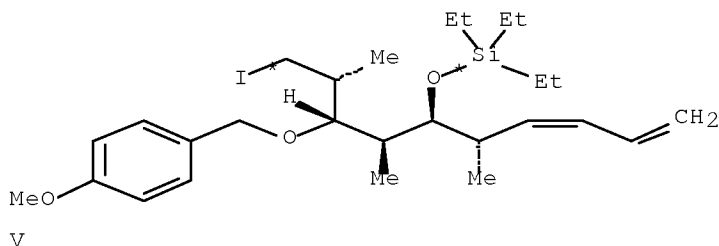
CON 0 deg C

PRO G 851889-86-6

NTE last stage quench

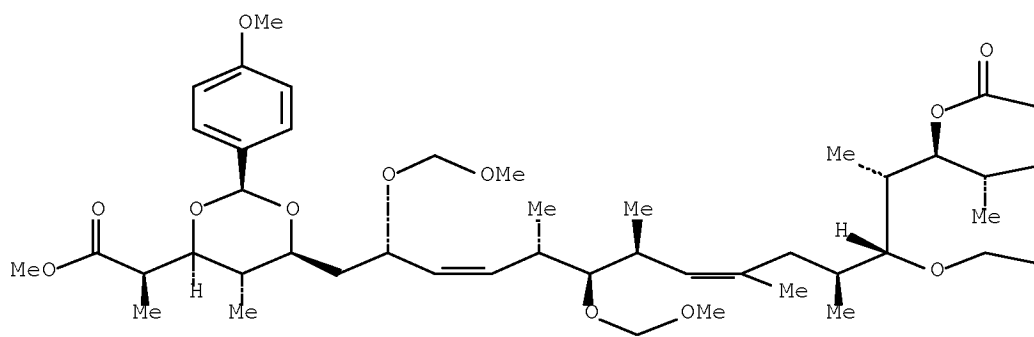
RX(150) OF 576 COMPOSED OF RX(35), RX(36), RX(2)

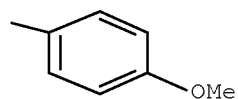
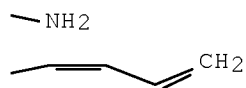
RX(150) V + O + H ==> I





PAGE 1-A





I
YIELD 95%

RX(35) RCT V 216669-69-1

STAGE(1)

SOL 60-29-7 Et2O

CON room temperature -> -78 deg C

STAGE(2)

RGT DK 594-19-4 t-BuLi

SOL 109-66-0 Pentane

CON 30 minutes, -78 deg C

STAGE(3)

RGT BO 7646-85-7 ZnCl2

SOL 109-99-9 THF

CON SUBSTAGE(1) 5 minutes, -78 deg C

SUBSTAGE(2) 30 minutes, -78 deg C -> 0 deg C

STAGE(4)

RCT O ~~851889-66-2~~

CAT 14221-01-3 Pd(PPh3)4

SOL 109-99-9 THF

CON SUBSTAGE(1) 1 hour, 0 deg C

SUBSTAGE(2) 0 deg C -> room temperature

SUBSTAGE(3) 6 hours, room temperature

STAGE(5)

SOL 7732-18-5 Water

CON room temperature

PRO DJ 851889-85-5

NTE last stage quench

RX(36) RCT DJ 851889-85-5

STAGE(1)

SOL 67-56-1 MeOH

CON room temperature -> 0 deg C

STAGE(2)

CAT 104-15-4 TsOH

CON 1 hour, 0 deg C

STAGE(3)

RGT AR 121-44-8 Et3N

CON 0 deg C

PRO G 851889-86-6

NTE last stage quench

RX(2) RCT G 851889-86-6

STAGE(1)

SOL 75-09-2 CH2Cl2

CON room temperature

STAGE(2)

RCT H 3019-71-4

CON 10 minutes, room temperature

STAGE(3)

SOL 67-56-1 MeOH

CON room temperature

STAGE(4)

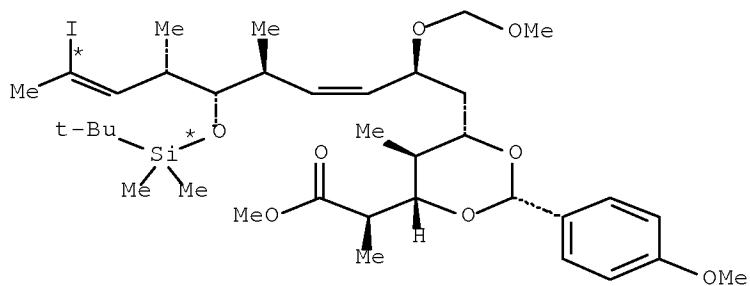
RGT J 584-08-7 K2CO3

CON 75 minutes, room temperature

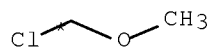
PRO I 851889-65-1

RX(151) OF 576 COMPOSED OF RX(3), RX(35), RX(36), RX(2)

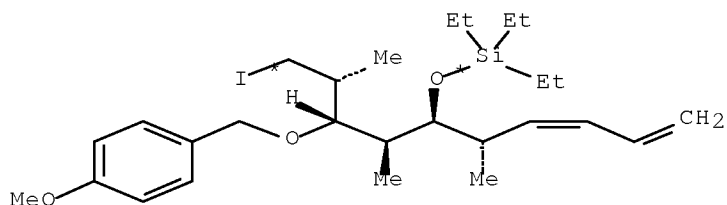
RX(151) M + N + V + H ==> I



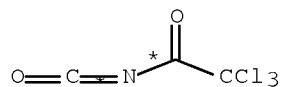
M



N



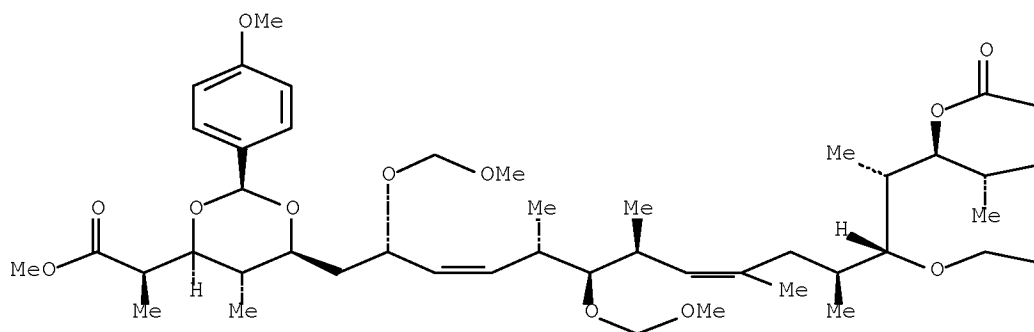
V



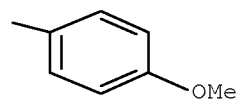
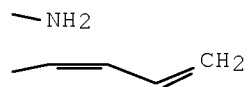
H

4
STEPS
→

PAGE 1-A



PAGE 1-B



I
YIELD 95%

RX(3) RCT M 851889-82-2

STAGE(1)

SOL 109-99-9 THF

CON room temperature

STAGE(2)

RGT P 64-19-7 AcOH, Q 429-41-4 Bu4N.F

SOL 109-99-9 THF
CON 36 hours, room temperature

STAGE(3)
SOL 7732-18-5 Water
CON room temperature, pH 7

STAGE(4)
RGT R 7087-68-5 EtN(Pr-i)2
SOL 56-23-5 CCl4
CON room temperature -> 0 deg C

STAGE(5)
CAT 1122-58-3 4-DMAP
CON 0 deg C

STAGE(6)
RCT N 107-30-2
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 8 hours, 0 deg C -> room temperature

STAGE(7)
RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water

PRO O 851889-66-2
NTE third stage quench

RX(35) RCT V 216669-69-1

STAGE(1)
SOL 60-29-7 Et2O
CON room temperature -> -78 deg C

STAGE(2)
RGT DK 594-19-4 t-BuLi
SOL 109-66-0 Pentane
CON 30 minutes, -78 deg C

STAGE(3)
RGT BO 7646-85-7 ZnCl2
SOL 109-99-9 THF
CON SUBSTAGE(1) 5 minutes, -78 deg C
SUBSTAGE(2) 30 minutes, -78 deg C -> 0 deg C

STAGE(4)
RCT O 851889-66-2
CAT 14221-01-3 Pd(PPh3)4
SOL 109-99-9 THF
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature
SUBSTAGE(3) 6 hours, room temperature

STAGE(5)
SOL 7732-18-5 Water
CON room temperature

PRO DJ 851889-85-5
NTE last stage quench

RX(36) RCT DJ 851889-85-5

STAGE(1)

SOL 67-56-1 MeOH

CON room temperature -> 0 deg C

STAGE(2)

CAT 104-15-4 TsOH

CON 1 hour, 0 deg C

STAGE(3)

RGT AR 121-44-8 Et3N

CON 0 deg C

PRO G 851889-86-6

NTE last stage quench

RX(2) RCT G 851889-86-6

STAGE(1)

SOL 75-09-2 CH2Cl2

CON room temperature

STAGE(2)

RCT H 3019-71-4

CON 10 minutes, room temperature

STAGE(3)

SOL 67-56-1 MeOH

CON room temperature

STAGE(4)

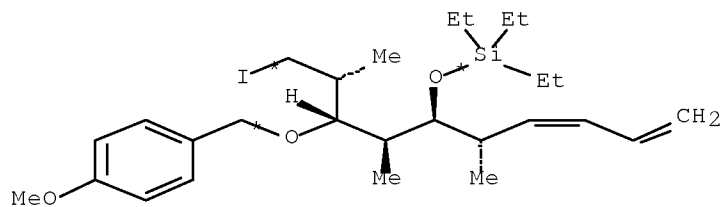
RGT J 584-08-7 K2CO3

CON 75 minutes, room temperature

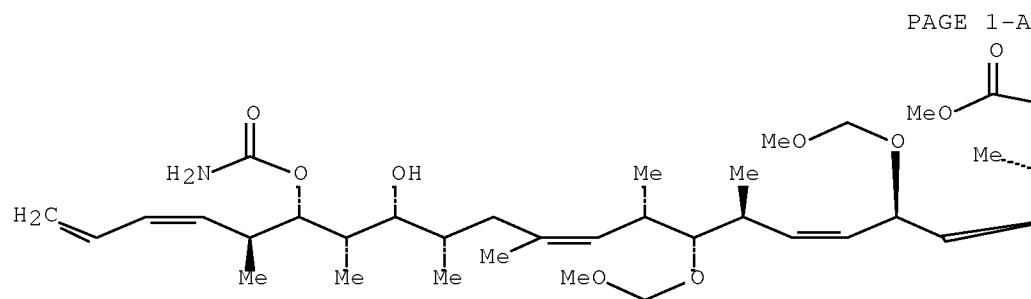
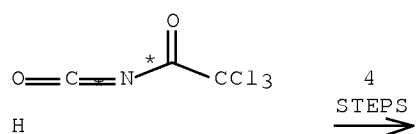
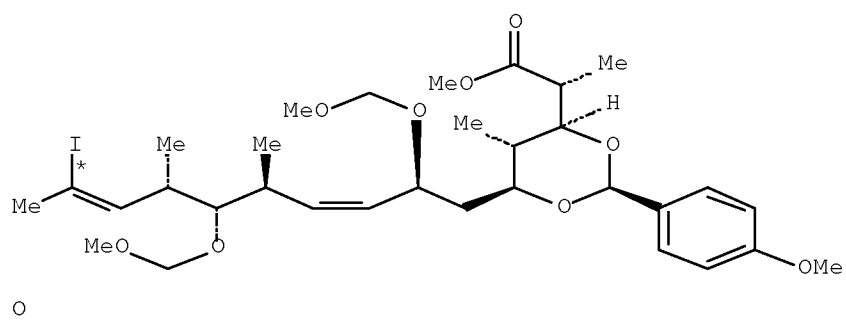
PRO I 851889-65-1

RX(154) OF 576 COMPOSED OF RX(35), RX(36), RX(2), RX(37)

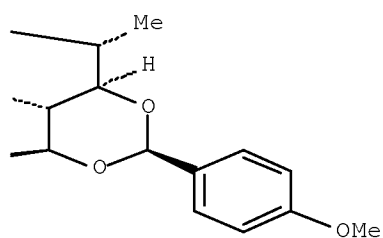
RX(154) V + C + H ==> A



V



PAGE 1-B



A
YIELD 90%

RX(35) RCT V 216669-69-1

STAGE(1)
SOL 60-29-7 Et2O
CON room temperature -> -78 deg C

STAGE(2)
RGT DK 594-19-4 t-BuLi
SOL 109-66-0 Pentane
CON 30 minutes, -78 deg C

STAGE(3)
RGT BO 7646-85-7 ZnCl2
SOL 109-99-9 THF
CON SUBSTAGE(1) 5 minutes, -78 deg C
SUBSTAGE(2) 30 minutes, -78 deg C -> 0 deg C

STAGE(4)
RCT O 851889-66-2
CAT 14221-01-3 Pd(PPh3)4
SOL 109-99-9 THF
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature
SUBSTAGE(3) 6 hours, room temperature

STAGE(5)
SOL 7732-18-5 Water
CON room temperature

PRO DJ 851889-85-5
NTE last stage quench

RX(36) RCT DJ 851889-85-5

STAGE(1)
SOL 67-56-1 MeOH
CON room temperature -> 0 deg C

STAGE(2)
CAT 104-15-4 TsOH
CON 1 hour, 0 deg C

STAGE(3)
RGT AR 121-44-8 Et3N
CON 0 deg C

PRO G 851889-86-6
NTE last stage quench

RX(2) RCT G 851889-86-6

STAGE(1)
SOL 75-09-2 CH2Cl2
CON room temperature

STAGE(2)
RCT H 3019-71-4
CON 10 minutes, room temperature

STAGE(3)

SOL 67-56-1 MeOH

CON room temperature

STAGE(4)

RGT J 584-08-7 K2CO3

CON 75 minutes, room temperature

PRO I 851889-65-1

RX(37) RCT I 851889-65-1

STAGE(1)

SOL 7732-18-5 Water, 75-09-2 CH2Cl2

CON room temperature

STAGE(2)

RGT D 144-55-8 NaHCO3

CON room temperature

STAGE(3)

RGT DM 84-58-2 DDQ

SOL 75-09-2 CH2Cl2

CON 1 hour, room temperature

STAGE(4)

RGT DM 84-58-2 DDQ

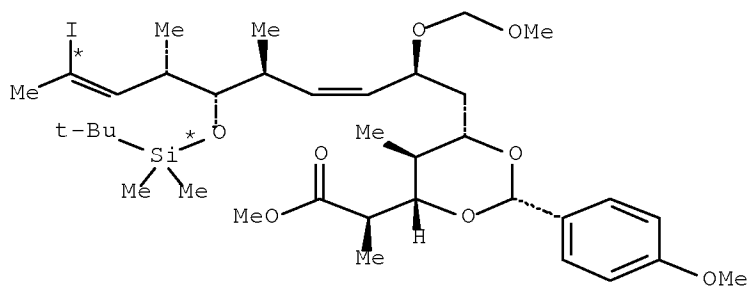
SOL 75-09-2 CH2Cl2

CON 1 hour, room temperature

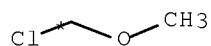
PRO A 851889-87-7

RX(157) OF 576 COMPOSED OF RX(3), RX(35), RX(36), RX(2), RX(37)

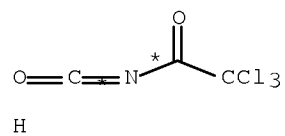
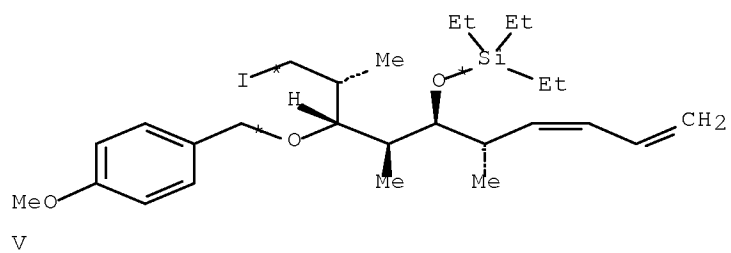
RX(157) M + N + V + H ==> A



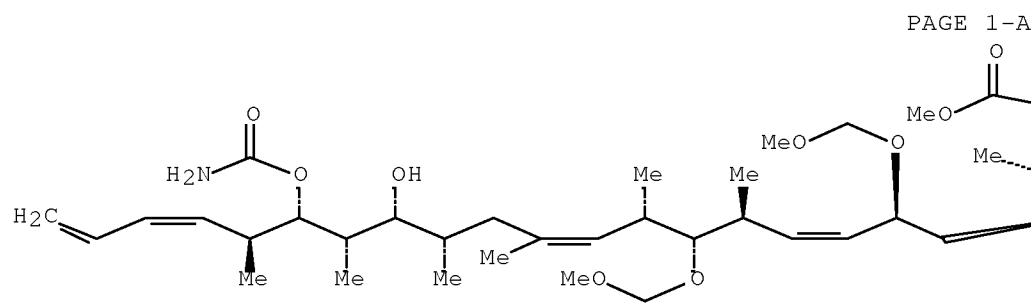
M



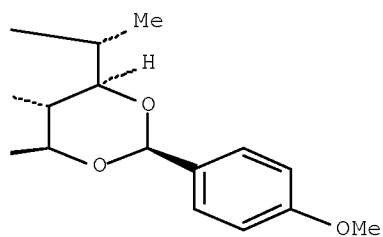
N



5
STEPS
→



PAGE 1-B



YIELD 90%

RX(3) RCT M 851889-82-2

STAGE(1)

SOL 109-99-9 THF
CON room temperature

STAGE(2)

RGT P 64-19-7 AcOH, Q 429-41-4 Bu4N.F
SOL 109-99-9 THF
CON 36 hours, room temperature

STAGE(3)

SOL 7732-18-5 Water
CON room temperature, pH 7

STAGE(4)

RGT R 7087-68-5 EtN(Pr-i)2
SOL 56-23-5 CCl4
CON room temperature -> 0 deg C

STAGE(5)

CAT 1122-58-3 4-DMAP
CON 0 deg C

STAGE(6)

RCT N 107-30-2
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 8 hours, 0 deg C -> room temperature

STAGE(7)

RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water

PRO O 851889-66-2
NTE third stage quench

RX(35) RCT V 216669-69-1

STAGE(1)

SOL 60-29-7 Et2O
CON room temperature -> -78 deg C

STAGE(2)

RGT DK 594-19-4 t-BuLi
SOL 109-66-0 Pentane
CON 30 minutes, -78 deg C

STAGE(3)

RGT BO 7646-85-7 ZnCl2
SOL 109-99-9 THF
CON SUBSTAGE(1) 5 minutes, -78 deg C
SUBSTAGE(2) 30 minutes, -78 deg C -> 0 deg C

STAGE(4)

RCT O 851889-66-2
CAT 14221-01-3 Pd(PPh3)4
SOL 109-99-9 THF
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature
SUBSTAGE(3) 6 hours, room temperature

STAGE(5)

SOL 7732-18-5 Water

```

        CON  room temperature

PRO  DJ 851889-85-5
NTE  last stage quench

RX(36)  RCT  DJ 851889-85-5

        STAGE(1)
        SOL  67-56-1 MeOH
        CON  room temperature -> 0 deg C

        STAGE(2)
        CAT  104-15-4 TsOH
        CON  1 hour, 0 deg C

        STAGE(3)
        RGT  AR 121-44-8 Et3N
        CON  0 deg C

PRO  G 851889-86-6
NTE  last stage quench

RX(2)  RCT  G 851889-86-6

        STAGE(1)
        SOL  75-09-2 CH2Cl2
        CON  room temperature

        STAGE(2)
        RCT  H 3019-71-4
        CON  10 minutes, room temperature

        STAGE(3)
        SOL  67-56-1 MeOH
        CON  room temperature

        STAGE(4)
        RGT  J 584-08-7 K2CO3
        CON  75 minutes, room temperature

PRO  I 851889-65-1

RX(37)  RCT  I 851889-65-1

        STAGE(1)
        SOL  7732-18-5 Water, 75-09-2 CH2Cl2
        CON  room temperature

        STAGE(2)
        RGT  D 144-55-8 NaHCO3
        CON  room temperature

        STAGE(3)
        RGT  DM 84-58-2 DDQ
        SOL  75-09-2 CH2Cl2
        CON  1 hour, room temperature

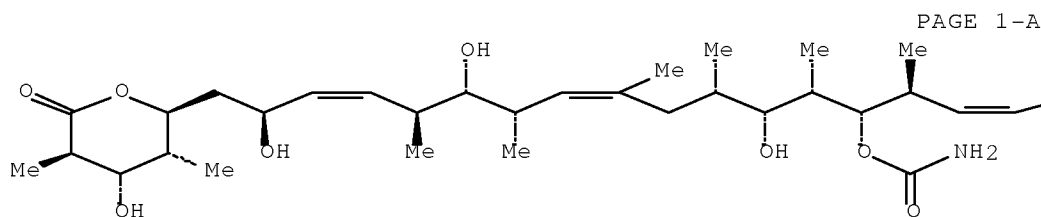
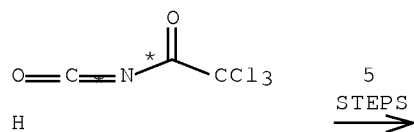
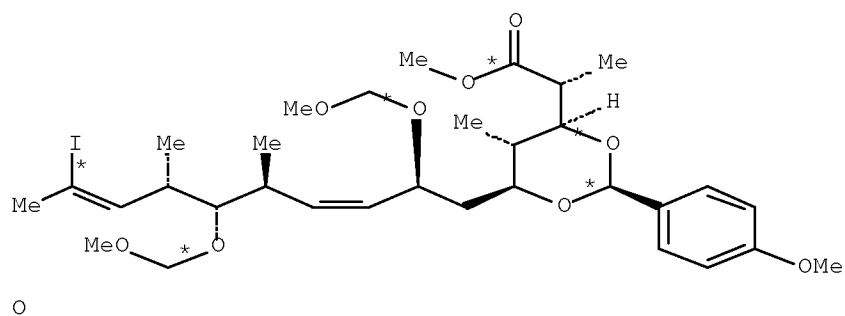
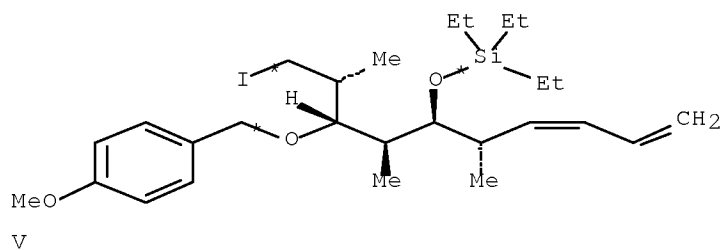
        STAGE(4)
        RGT  DM 84-58-2 DDQ
        SOL  75-09-2 CH2Cl2

```

CON 1 hour, room temperature

PRO A 851889-87-7

RX(313) OF 576 COMPOSED OF RX(35), RX(36), RX(2), RX(37), RX(1)
 RX(313) V + G + H ==> B





^B
YIELD 69%

RX(35) RCT V 216669--69--1

STAGE(1)

SOL 60-29-7 Et2O
CON room temperature -> -78 deg C

STAGE(2)

RGT DK 594-19-4 t-BuLi
SOL 109-66-0 Pentane
CON 30 minutes, -78 deg C

STAGE(3)

RGT BO 7646-85-7 ZnCl2
SOL 109-99-9 THF
CON SUBSTAGE(1) 5 minutes, -78 deg C
SUBSTAGE(2) 30 minutes, -78 deg C -> 0 deg C

STAGE(4)

RCT O 851889-66--2
CAT 14221-01-3 Pd(PPh3)4
SOL 109-99-9 THF
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature
SUBSTAGE(3) 6 hours, room temperature

STAGE(5)

SOL 7732-18-5 Water
CON room temperature

PRO DJ 851889-85-5

NTE last stage quench

RX(36) RCT DJ 851889-85-5

STAGE(1)

SOL 67-56-1 MeOH
CON room temperature -> 0 deg C

STAGE(2)

CAT 104-15-4 TsOH
CON 1 hour, 0 deg C

STAGE(3)

RGT AR 121-44-8 Et3N
CON 0 deg C

PRO G 851889-86-6
NTE last stage quench

RX(2) RCT G 851889-86-6

STAGE(1)
SOL 75-09-2 CH₂Cl₂
CON room temperature

STAGE(2)
RCT H 3019-71-4
CON 10 minutes, room temperature

STAGE(3)
SOL 67-56-1 MeOH
CON room temperature

STAGE(4)
RGT J 584-08-7 K₂CO₃
CON 75 minutes, room temperature

PRO I 851889-65-1

RX(37) RCT I 851889-65-1

STAGE(1)
SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
CON room temperature

STAGE(2)
RGT D 144-55-8 NaHCO₃
CON room temperature

STAGE(3)
RGT DM 84-58-2 DDQ
SOL 75-09-2 CH₂Cl₂
CON 1 hour, room temperature

STAGE(4)
RGT DM 84-58-2 DDQ
SOL 75-09-2 CH₂Cl₂
CON 1 hour, room temperature

PRO A 851889-87-7

RX(1) RCT A 851889-87-7

STAGE(1)
SOL 109-99-9 THF
CON room temperature

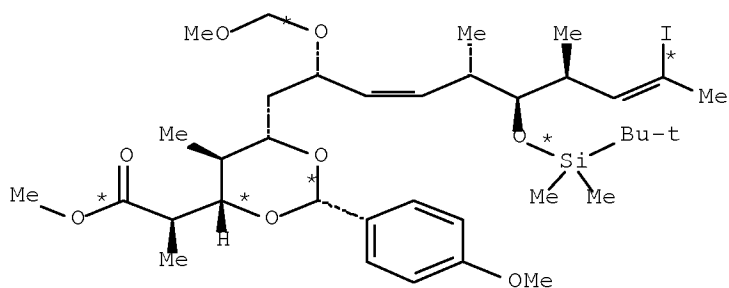
STAGE(2)
RGT C 7647-01-0 HCl
SOL 7732-18-5 Water
CON 70 hours, room temperature

STAGE(3)
RGT D 144-55-8 NaHCO₃
SOL 7732-18-5 Water

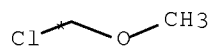
CON room temperature

PRO B 127943-53-7

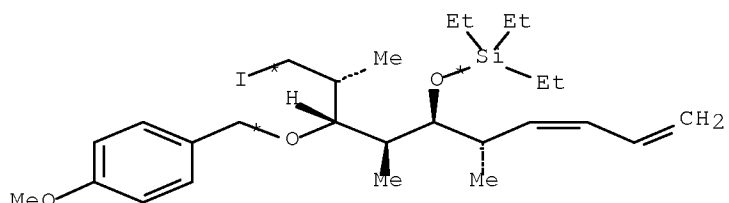
RX(314) OF 576 COMPOSED OF RX(3), RX(35), RX(36), RX(2), RX(37), RX(1)
 RX(314) M + N + V + H ==> B



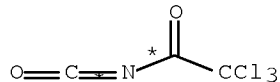
M



N

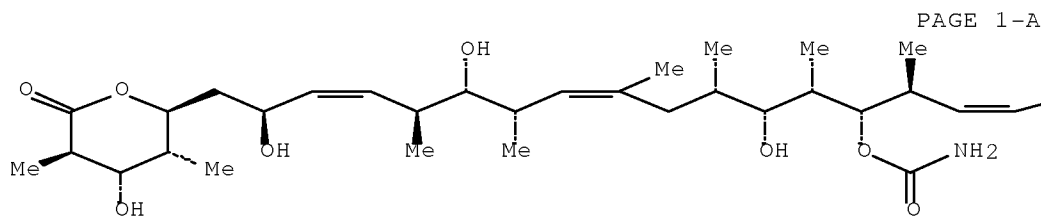


V



H

6
 STEPS
 →



PAGE 1-A



^B
YIELD 69%

RX(3) RCT M 851889-82-2

STAGE(1)

SOL 109-99-9 THF
CON room temperature

STAGE(2)

RGT P 64-19-7 AcOH, Q 429-41-4 Bu₄N.F
SOL 109-99-9 THF
CON 36 hours, room temperature

STAGE(3)

SOL 7732-18-5 Water
CON room temperature, pH 7

STAGE(4)

RGT R 7087-68-5 EtN(Pr-i)₂
SOL 56-23-5 CCl₄
CON room temperature -> 0 deg C

STAGE(5)

CAT 1122-58-3 4-DMAP
CON 0 deg C

STAGE(6)

RCT N 107-30-2
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 8 hours, 0 deg C -> room temperature

STAGE(7)

RGT D 144-55-8 NaHCO₃
SOL 7732-18-5 Water

PRO O 851889-66-2

NTE third stage quench

RX(35) RCT V 216669-69-1

STAGE(1)

SOL 60-29-7 Et₂O
CON room temperature -> -78 deg C

STAGE(2)

RGT DK 594-19-4 t-BuLi
SOL 109-66-0 Pentane
CON 30 minutes, -78 deg C

STAGE(3)
RGT BO 7646-85-7 ZnCl2
SOL 109-99-9 THF
CON SUBSTAGE(1) 5 minutes, -78 deg C
SUBSTAGE(2) 30 minutes, -78 deg C -> 0 deg C

STAGE(4)
RCT O 851889-66-2
CAT 14221-01-3 Pd(PPh3)4
SOL 109-99-9 THF
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature
SUBSTAGE(3) 6 hours, room temperature

STAGE(5)
SOL 7732-18-5 Water
CON room temperature

PRO DJ 851889-85-5
NTE last stage quench

RX(36) RCT DJ 851889-85-5

STAGE(1)
SOL 67-56-1 MeOH
CON room temperature -> 0 deg C

STAGE(2)
CAT 104-15-4 TsOH
CON 1 hour, 0 deg C

STAGE(3)
RGT AR 121-44-8 Et3N
CON 0 deg C

PRO G 851889-86-6
NTE last stage quench

RX(2) RCT G 851889-86-6

STAGE(1)
SOL 75-09-2 CH2Cl2
CON room temperature

STAGE(2)
RCT H 3019-71-4
CON 10 minutes, room temperature

STAGE(3)
SOL 67-56-1 MeOH
CON room temperature

STAGE(4)
RGT J 584-08-7 K2CO3
CON 75 minutes, room temperature

PRO I 851889-65-1

RX(37) RCT I 851889-65-1

STAGE(1)
SOL 7732-18-5 Water, 75-09-2 CH2Cl2
CON room temperature

STAGE(2)
RGT D 144-55-8 NaHCO3
CON room temperature

STAGE(3)
RGT DM 84-58-2 DDQ
SOL 75-09-2 CH2Cl2
CON 1 hour, room temperature

STAGE(4)
RGT DM 84-58-2 DDQ
SOL 75-09-2 CH2Cl2
CON 1 hour, room temperature

PRO A 851889-87-7

RX(1) RCT A 851889-87-7

STAGE(1)
SOL 109-99-9 THF
CON room temperature

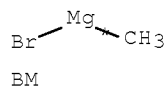
STAGE(2)
RGT C 7647-01-0 HCl
SOL 7732-18-5 Water
CON 70 hours, room temperature

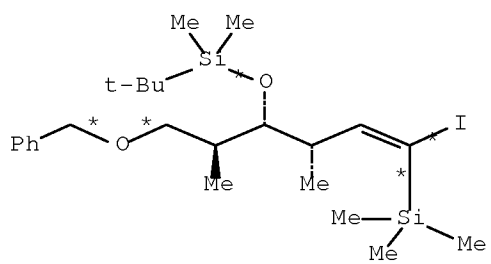
STAGE(3)
RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water
CON room temperature

PRO B 127943-53-7

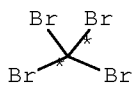
RX(382) OF 576 COMPOSED OF RX(15), RX(16), RX(17), RX(18), RX(6), RX(28),
RX(29), RX(30), RX(32), RX(33), RX(34), RX(3), RX(35)

RX(382) BM + BK + BF + AF + AA + CM + CT + 2 N +
V ==> DJ

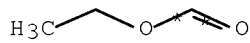




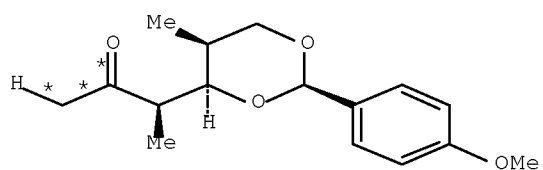
BK



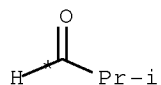
BF



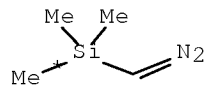
AF



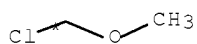
AA



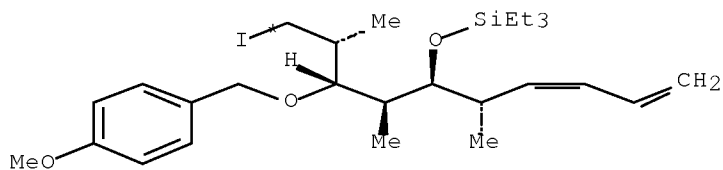
CM



CT

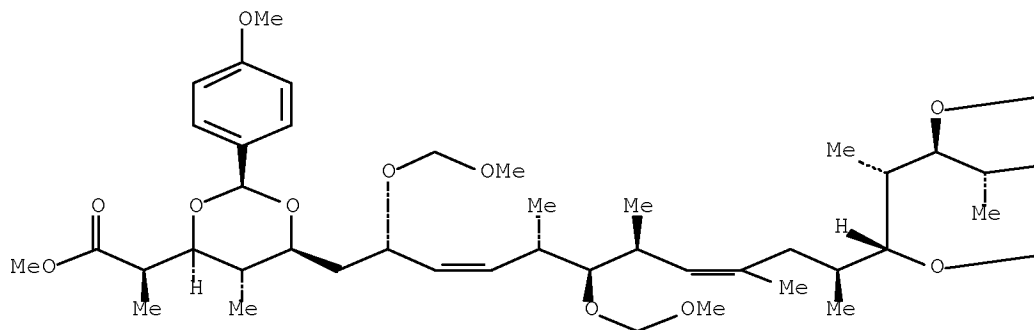


2 N



V

13
STEPS
→



* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

RX(15)

STAGE(1)

RGT BO 7646-85-7 ZnCl₂
 SOL 109-99-9 THF
 CON room temperature

STAGE(2)

RCT BM 75-16-1
 SOL 60-29-7 Et₂O
 CON 15 minutes, room temperature

STAGE(3)

RCT BK 444109-29-9
 CAT 14221-01-3 Pd(PPh₃)₄
 SOL 109-99-9 THF
 CON 2 hours, room temperature

STAGE(4)

RGT AI 12125-02-9 NH₄Cl
 SOL 7732-18-5 Water
 CON room temperature

PRO BN 444109-30-2

NTE key step, stereoselective; last stage quench

RX(16)

STAGE(1)

RGT BS 1625-91-8 (p-t-BuC₆H₄)₂
 SOL 109-99-9 THF
 CON room temperature

STAGE(2)

RGT BT 7439-93-2 Li
 CON SUBSTAGE(1) room temperature
 SUBSTAGE(2) room temperature -> 25 deg C
 SUBSTAGE(3) 5 hours, 15 - 25 deg C
 SUBSTAGE(4) 15 deg C -> room temperature

STAGE(3)
RCT BN 444109-30-2
SOL 109-99-9 THF
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) 2.5 hours, -78 deg C

STAGE(4)
RGT AI 12125-02-9 NH4Cl
SOL 7732-18-5 Water
CON -78 deg C -> room temperature

PRO BR 444109-31-3
NTE first stage sonication; third stage inverse addn.; last stage
quench

RX(17)

STAGE(1)
RGT AQ 79-37-8 (COCl)₂
SOL 75-09-2 CH₂Cl₂
CON room temperature -> -78 deg C

STAGE(2)
RGT AP 67-68-5 DMSO
CON 45 minutes, -78 deg C

STAGE(3)
RCT BR 444109-31-3
SOL 75-09-2 CH₂Cl₂
CON 1 hour, -78 deg C

STAGE(4)
RGT AR 121-44-8 Et₃N
CON SUBSTAGE(1) 15 minutes, -78 deg C
SUBSTAGE(2) 20 minutes, -78 deg C -> room temperature

PRO BU 444109-43-7
NTE last stage quench; Swern oxidn.

RX(18) RCT BF 558-13-4

STAGE(1)
RGT W 603-35-0 PPh₃
SOL 75-09-2 CH₂Cl₂
CON 10 minutes, 0 deg C

STAGE(2)
RCT BU 444109-43-7
RGT BH 108-48-5 2,6-Lutidine
SOL 75-09-2 CH₂Cl₂
CON 4 hours, 0 deg C

STAGE(3)
RGT AI 12125-02-9 NH₄Cl
SOL 7732-18-5 Water
CON 0 deg C

PRO AE 444109-32-4
NTE last stage quench; Corey-Fuchs olefination

RX(6) RCT AE 444109-32-4

STAGE(1)

SOL 109-99-9 THF
CON room temperature -> -78 deg C

STAGE(2)

RGT AH 109-72-8 BuLi
SOL 110-54-3 Hexane
CON SUBSTAGE(1) 30 minutes, -78 deg C
SUBSTAGE(2) -78 deg C -> -20 deg C
SUBSTAGE(3) 1 hour, -20 deg C
SUBSTAGE(4) -20 deg C -> -78 deg C

STAGE(3)

RCT AF 109-94-4
CON SUBSTAGE(1) 2 hours, -78 deg C
SUBSTAGE(2) -78 deg C -> 30 deg C
SUBSTAGE(3) 8 hours, 30 deg C

STAGE(4)

RGT AI 12125-02-9 NH4Cl
SOL 7732-18-5 Water
CON 30 deg C -> room temperature

PRO AG 444109-23-3
NTE last stage quench

RX(28) RCT AA 652986-45-3

STAGE(1)

SOL 75-09-2 CH2Cl2
CON room temperature -> -78 deg C

STAGE(2)

RGT R 7087-68-5 EtN(Pr-i)2
CON 5 minutes, -78 deg C

STAGE(3)

RGT CK 60669-69-4 F3CSO3BBu2
CON 45 minutes, -78 deg C

STAGE(4)

RCT AG 444109-23-3
SOL 75-09-2 CH2Cl2
CON 1 hour, -78 deg C

STAGE(5)

SOL 7732-18-5 Water, 67-56-1 MeOH
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> 0 deg C

STAGE(6)

RGT CL 7722-84-1 H2O2
SOL 7732-18-5 Water, 67-56-1 MeOH
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature

STAGE(7)

RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water
CON room temperature

PRO CJ 851889-73-1
NTE key step, stereoselective (d.r. 30:1); fifth stage phosphate
buffer; aldol reaction

RX(29) RCT CJ 851889-73-1

STAGE(1)
SOL 109-99-9 THF
CON room temperature

STAGE(2)
RCT CM 78-84-2
CON room temperature -> -10 deg C

STAGE(3)
RGT CO 32248-43-4 SmI2
SOL 109-99-9 THF
CON 4 hours, -10 deg C

STAGE(4)
RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water
CON -10 deg C -> room temperature

PRO CN 851889-75-3
NTE last stage quench

RX(30) RCT CN 851889-75-3

STAGE(1)
SOL 67-56-1 MeOH
CON room temperature

STAGE(2)
RGT CR 1310-58-3 KOH
CON room temperature

PRO CP 851889-76-4, CQ 851889-77-5
NTE reaction monitored by TLC

RX(32) RCT CP 851889-76-4

STAGE(1)
SOL 71-43-2 Benzene
CON room temperature

STAGE(2)
CAT 15529-49-4 RuCl2(PPh3)3
CON 2 hours, room temperature

STAGE(3)
CAT 15529-49-4 RuCl2(PPh3)3
CON 6 hours, room temperature

STAGE(4)
RGT CV 513-35-9 Me2C:CHMe

SOL 75-65-0 t-BuOH
CON room temperature

STAGE(5)

RGT CW 7558-80-7 NaH₂PO₄, CX 7758-19-2 NaOClO
SOL 7732-18-5 Water
CON 1 hour, room temperature

STAGE(6)

RGT CW 7558-80-7 NaH₂PO₄, CX 7758-19-2 NaOClO
SOL 7732-18-5 Water
CON 1 hour, room temperature

STAGE(7)

SOL 60-29-7 Et₂O
CON room temperature

STAGE(8)

RGT C 7647-01-0 HCl
SOL 7732-18-5 Water
CON room temperature

STAGE(9)

SOL 67-56-1 MeOH, 71-43-2 Benzene
CON room temperature

STAGE(10)

RCT CT 18107-18-1
SOL 110-54-3 Hexane
CON 15 minutes, room temperature

PRO CU 851889-79-7
NTE last stage acidification

RX(33) RCT CU 851889-79-7

STAGE(1)

RGT R 7087-68-5 EtN(Pr-i)₂
SOL 75-09-2 CH₂Cl₂
CON room temperature -> 0 deg C

STAGE(2)

CAT 1122-58-3 4-DMAP
CON 0 deg C

STAGE(3)

RCT N 107-30-2
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 8 hours, 0 deg C -> room temperature

STAGE(4)

RGT D 144-55-8 NaHCO₃
SOL 7732-18-5 Water

PRO DB 851889-80-0

RX(34) RCT DB 851889-80-0

STAGE(1)

SOL 110-54-3 Hexane

CON room temperature

STAGE(2)

CAT 91-22-5 Quinoline

CON room temperature

STAGE(3)

CAT 7440-05-3 Pd

CON room temperature

STAGE(4)

RGT DC 1333-74-0 H2

CON 8 hours, room temperature

STAGE(5)

SOL 107-14-2 ClCH2CN, 75-05-8 MeCN

CON room temperature

STAGE(6)

RGT DD 516-12-1 Iodosuccinimide

CON 3 hours, room temperature

STAGE(7)

RGT DE 7772-98-7 Na2S2O3

SOL 7732-18-5 Water

CON room temperature

PRO M 851889-82-2

NTE stereoselective; third stage Lindlar catalyst; sixth stage in dark; last stage quench

RX(3)

RCT M 851889-82-2

STAGE(1)

SOL 109-99-9 THF

CON room temperature

STAGE(2)

RGT P 64-19-7 AcOH, Q 429-41-4 Bu4N.F

SOL 109-99-9 THF

CON 36 hours, room temperature

STAGE(3)

SOL 7732-18-5 Water

CON room temperature, pH 7

STAGE(4)

RGT R 7087-68-5 EtN(Pr-i)2

SOL 56-23-5 CCl4

CON room temperature -> 0 deg C

STAGE(5)

CAT 1122-58-3 4-DMAP

CON 0 deg C

STAGE(6)

RCT N 107-30-2

CON SUBSTAGE(1) 0 deg C

SUBSTAGE(2) 8 hours, 0 deg C -> room temperature

STAGE(7)

RGT D 144-55-8 NaHCO3

SOL 7732-18-5 Water

PRO O 851889-66-2

NTE third stage quench

RX(35) RCT V 216669-69-1

STAGE(1)

SOL 60-29-7 Et2O

CON room temperature -> -78 deg C

STAGE(2)

RGT DK 594-19-4 t-BuLi

SOL 109-66-0 Pentane

CON 30 minutes, -78 deg C

STAGE(3)

RGT BO 7646-85-7 ZnCl2

SOL 109-99-9 THF

CON SUBSTAGE(1) 5 minutes, -78 deg C

SUBSTAGE(2) 30 minutes, -78 deg C -> 0 deg C

STAGE(4)

RCT O 851889-66-2

CAT 14221-01-3 Pd(PPh3)4

SOL 109-99-9 THF

CON SUBSTAGE(1) 1 hour, 0 deg C

SUBSTAGE(2) 0 deg C -> room temperature

SUBSTAGE(3) 6 hours, room temperature

STAGE(5)

SOL 7732-18-5 Water

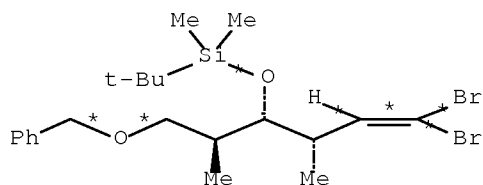
CON room temperature

PRO DJ 851889-85-5

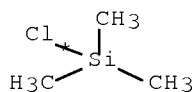
NTE last stage quench

RX(398) OF 576 COMPOSED OF RX(13), RX(14), RX(15), RX(16), RX(17), RX(18),
 RX(6), RX(28), RX(29), RX(30), RX(32), RX(33), RX(34), RX(3), RX(35)

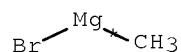
RX(398) BG + BI + BM + BF + AF + AA + CM + CT + 2 N
 + V ==> DJ



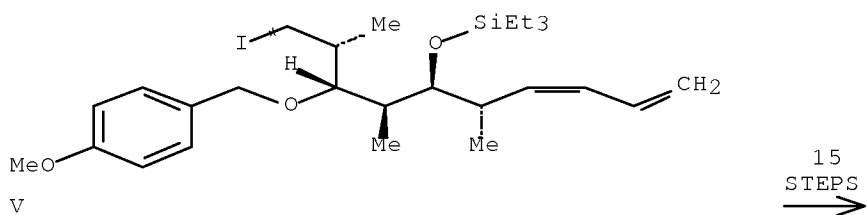
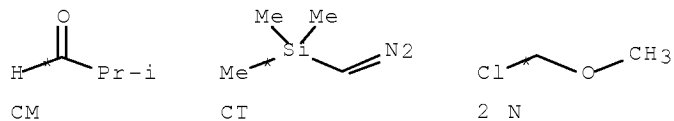
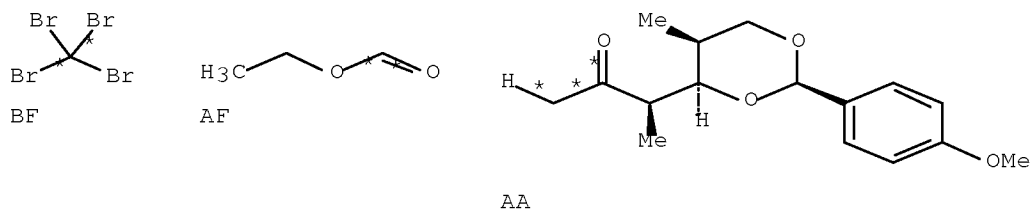
BG



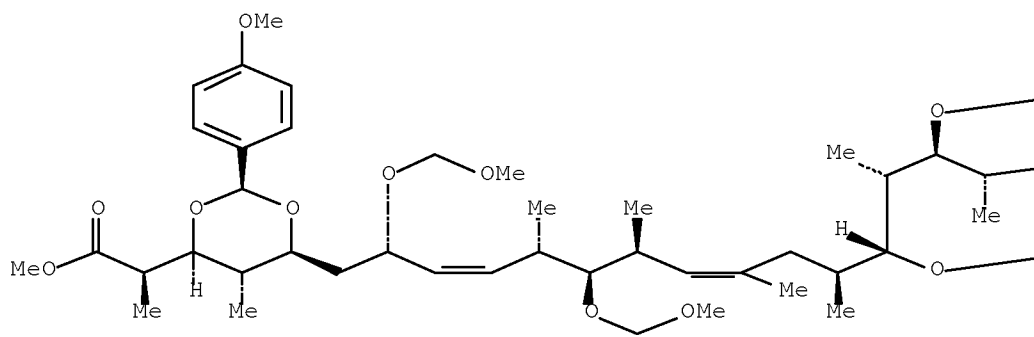
BI



BM



PAGE 1-A



* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

RX(13) RCT BG 444109-27-7

STAGE(1)

SOL 109-99-9 THF
CON room temperature -> -78 deg C

STAGE(2)

RGT AH 109-72-8 BuLi
SOL 110-54-3 Hexane
CON SUBSTAGE(1) 1 hour, -78 deg C
SUBSTAGE(2) -78 deg C -> -20 deg C
SUBSTAGE(3) 1 hour, -20 deg C
SUBSTAGE(4) -20 deg C -> -78 deg C

STAGE(3)

RCT BI 75-77-4
CON 8 hours, -78 deg C -> room temperature

STAGE(4)

RGT AI 12125-02-9 NH4Cl
SOL 7732-18-5 Water

PRO BJ 444109-28-8

RX(14) RCT BJ 444109-28-8

STAGE(1)

SOL 109-99-9 THF
CON room temperature

STAGE(2)

RGT BL 37342-97-5 Hydrozirconocene Cl
CON SUBSTAGE(1) 5 minutes, room temperature
SUBSTAGE(2) room temperature -> 55 deg C
SUBSTAGE(3) 1 hour, 55 deg C
SUBSTAGE(4) 55 deg C -> room temperature

STAGE(3)

RGT X 7553-56-2 I2
SOL 109-99-9 THF
CON 20 minutes, room temperature

PRO BK 444109-29-9

RX(15)

STAGE(1)

RGT BO 7646-85-7 ZnCl2
SOL 109-99-9 THF
CON room temperature

STAGE(2)

RCT BM 75-16-1
SOL 60-29-7 Et2O
CON 15 minutes, room temperature

STAGE(3)

RCT BK 444109-29-9
CAT 14221-01-3 Pd(PPh3)4
SOL 109-99-9 THF
CON 2 hours, room temperature

STAGE(4)

RGT AI 12125-02-9 NH4Cl
SOL 7732-18-5 Water
CON room temperature

PRO BN 444109-30-2
NTE key step, stereoselective; last stage quench

RX(16)

STAGE(1)
RGT BS 1625-91-8 (p-t-BuC6H4)2
SOL 109-99-9 THF
CON room temperature

STAGE(2)
RGT BT 7439-93-2 Li
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) room temperature -> 25 deg C
SUBSTAGE(3) 5 hours, 15 - 25 deg C
SUBSTAGE(4) 15 deg C -> room temperature

STAGE(3)
RCT BN 444109-30-2
SOL 109-99-9 THF
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) 2.5 hours, -78 deg C

STAGE(4)
RGT AI 12125-02-9 NH4Cl
SOL 7732-18-5 Water
CON -78 deg C -> room temperature

PRO BR 444109-31-3
NTE first stage sonication; third stage inverse addn.; last stage quench

RX(17)

STAGE(1)
RGT AQ 79-37-8 (COCl)2
SOL 75-09-2 CH2Cl2
CON room temperature -> -78 deg C

STAGE(2)
RGT AP 67-68-5 DMSO
CON 45 minutes, -78 deg C

STAGE(3)
RCT BR 444109-31-3
SOL 75-09-2 CH2Cl2
CON 1 hour, -78 deg C

STAGE(4)
RGT AR 121-44-8 Et3N
CON SUBSTAGE(1) 15 minutes, -78 deg C
SUBSTAGE(2) 20 minutes, -78 deg C -> room temperature

PRO BU 444109-43-7
NTE last stage quench; Swern oxidn.

RX(18) RCT BF 558-13-4

 STAGE(1)
 RGT W 603-35-0 PPh3
 SOL 75-09-2 CH2Cl2
 CON 10 minutes, 0 deg C

 STAGE(2)
 RCT BU 444109-43-7
 RGT BH 108-48-5 2,6-Lutidine
 SOL 75-09-2 CH2Cl2
 CON 4 hours, 0 deg C

 STAGE(3)
 RGT AI 12125-02-9 NH4Cl
 SOL 7732-18-5 Water
 CON 0 deg C

PRO AE 444109-32-4
NTE last stage quench; Corey-Fuchs olefination

RX(6) RCT AE 444109-32-4

 STAGE(1)
 SOL 109-99-9 THF
 CON room temperature -> -78 deg C

 STAGE(2)
 RGT AH 109-72-8 BuLi
 SOL 110-54-3 Hexane
 CON SUBSTAGE(1) 30 minutes, -78 deg C
 SUBSTAGE(2) -78 deg C -> -20 deg C
 SUBSTAGE(3) 1 hour, -20 deg C
 SUBSTAGE(4) -20 deg C -> -78 deg C

 STAGE(3)
 RCT AF 109-94-4
 CON SUBSTAGE(1) 2 hours, -78 deg C
 SUBSTAGE(2) -78 deg C -> 30 deg C
 SUBSTAGE(3) 8 hours, 30 deg C

 STAGE(4)
 RGT AI 12125-02-9 NH4Cl
 SOL 7732-18-5 Water
 CON 30 deg C -> room temperature

PRO AG 444109-23-3
NTE last stage quench

RX(28) RCT AA 652986-45-3

 STAGE(1)
 SOL 75-09-2 CH2Cl2
 CON room temperature -> -78 deg C

 STAGE(2)
 RGT R 7087-68-5 EtN(Pr-i)2
 CON 5 minutes, -78 deg C

 STAGE(3)

RGT CK 60669-69-4 F3CSO3BBu2
CON 45 minutes, -78 deg C

STAGE(4)

RCT AG 444109-23-3
SOL 75-09-2 CH2Cl2
CON 1 hour, -78 deg C

STAGE(5)

SOL 7732-18-5 Water, 67-56-1 MeOH
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> 0 deg C

STAGE(6)

RGT CL 7722-84-1 H2O2
SOL 7732-18-5 Water, 67-56-1 MeOH
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature

STAGE(7)

RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water
CON room temperature

PRO CJ 851889-73-1

NTE key step, stereoselective (d.r. 30:1); fifth stage phosphate
buffer; aldol reaction

RX(29) RCT CJ 851889-73-1

STAGE(1)

SOL 109-99-9 THF
CON room temperature

STAGE(2)

RCT CM 78-84-2
CON room temperature -> -10 deg C

STAGE(3)

RGT CO 32248-43-4 SmI2
SOL 109-99-9 THF
CON 4 hours, -10 deg C

STAGE(4)

RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water
CON -10 deg C -> room temperature

PRO CN 851889-75-3

NTE last stage quench

RX(30) RCT CN 851889-75-3

STAGE(1)

SOL 67-56-1 MeOH
CON room temperature

STAGE(2)

RGT CR 1310-58-3 KOH
CON room temperature

PRO CP 851889-76-4, CQ 851889-77-5
NTE reaction monitored by TLC

RX(32) RCT CP 851889-76-4

STAGE(1)

SOL 71-43-2 Benzene
CON room temperature

STAGE(2)

CAT 15529-49-4 RuCl₂(PPh₃)₃
CON 2 hours, room temperature

STAGE(3)

CAT 15529-49-4 RuCl₂(PPh₃)₃
CON 6 hours, room temperature

STAGE(4)

RGT CV 513-35-9 Me₂C:CHMe
SOL 75-65-0 t-BuOH
CON room temperature

STAGE(5)

RGT CW 7558-80-7 NaH₂PO₄, CX 7758-19-2 NaOClO
SOL 7732-18-5 Water
CON 1 hour, room temperature

STAGE(6)

RGT CW 7558-80-7 NaH₂PO₄, CX 7758-19-2 NaOClO
SOL 7732-18-5 Water
CON 1 hour, room temperature

STAGE(7)

SOL 60-29-7 Et₂O
CON room temperature

STAGE(8)

RGT C 7647-01-0 HCl
SOL 7732-18-5 Water
CON room temperature

STAGE(9)

SOL 67-56-1 MeOH, 71-43-2 Benzene
CON room temperature

STAGE(10)

RCT CT 18107-18-1
SOL 110-54-3 Hexane
CON 15 minutes, room temperature

PRO CU 851889-79-7
NTE last stage acidification

RX(33) RCT CU 851889-79-7

STAGE(1)

RGT R 7087-68-5 EtN(Pr-i)₂
SOL 75-09-2 CH₂Cl₂
CON room temperature -> 0 deg C


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STAGE(2)
  CAT  1122-58-3 4-DMAP
  CON  0 deg C

STAGE(3)
  RCT  N 107-30-2
  CON  SUBSTAGE(1) 0 deg C
        SUBSTAGE(2) 8 hours, 0 deg C -> room temperature

STAGE(4)
  RGT  D 144-55-8 NaHCO3
  SOL  7732-18-5 Water

PRO   DB 851889-80-0

RX(34)  RCT  DB 851889-80-0

  STAGE(1)
    SOL  110-54-3 Hexane
    CON  room temperature

  STAGE(2)
    CAT  91-22-5 Quinoline
    CON  room temperature

  STAGE(3)
    CAT  7440-05-3 Pd
    CON  room temperature

  STAGE(4)
    RGT  DC 1333-74-0 H2
    CON  8 hours, room temperature

  STAGE(5)
    SOL  107-14-2 ClCH2CN, 75-05-8 MeCN
    CON  room temperature

  STAGE(6)
    RGT  DD 516-12-1 Iodosuccinimide
    CON  3 hours, room temperature

  STAGE(7)
    RGT  DE 7772-98-7 Na2S2O3
    SOL  7732-18-5 Water
    CON  room temperature

PRO   M 851889-82-2
NTE   stereoselective; third stage Lindlar catalyst; sixth stage in
      dark; last stage quench

RX(3)  RCT  M 851889-82-2

  STAGE(1)
    SOL  109-99-9 THF
    CON  room temperature

  STAGE(2)
    RGT  P 64-19-7 AcOH, Q 429-41-4 Bu4N.F
    SOL  109-99-9 THF

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CON 36 hours, room temperature

STAGE(3)
 SOL 7732-18-5 Water
 CON room temperature, pH 7

STAGE(4)
 RGT R 7087-68-5 EtN(Pr-i)2
 SOL 56-23-5 CCl4
 CON room temperature -> 0 deg C

STAGE(5)
 CAT 1122-58-3 4-DMAP
 CON 0 deg C

STAGE(6)
 RCT N 107-30-2
 CON SUBSTAGE(1) 0 deg C
 SUBSTAGE(2) 8 hours, 0 deg C -> room temperature

STAGE(7)
 RGT D 144-55-8 NaHCO3
 SOL 7732-18-5 Water

PRO O 851889-66-2
 NTE third stage quench

RX(35) RCT V 216669-69-1

STAGE(1)
 SOL 60-29-7 Et2O
 CON room temperature -> -78 deg C

STAGE(2)
 RGT DK 594-19-4 t-BuLi
 SOL 109-66-0 Pentane
 CON 30 minutes, -78 deg C

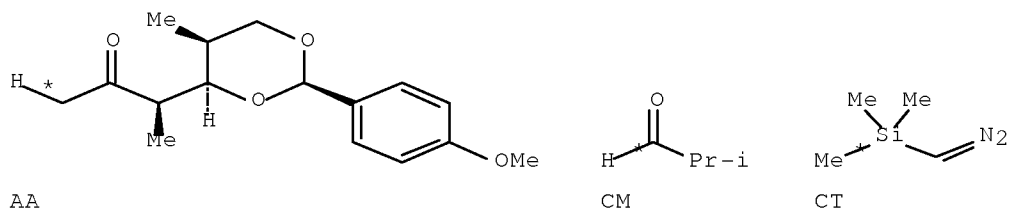
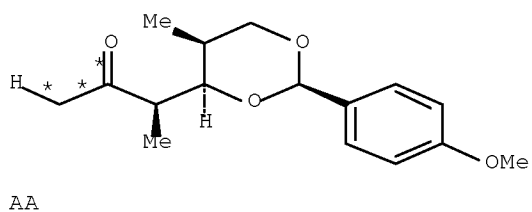
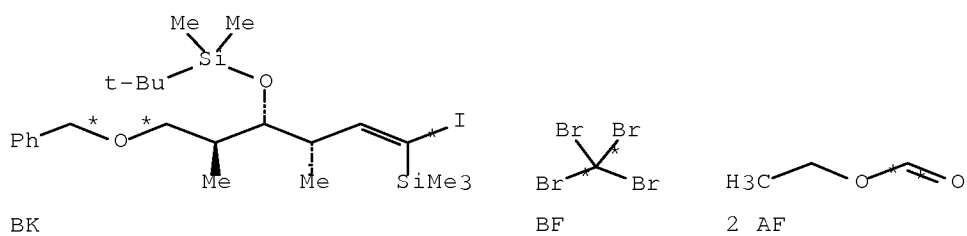
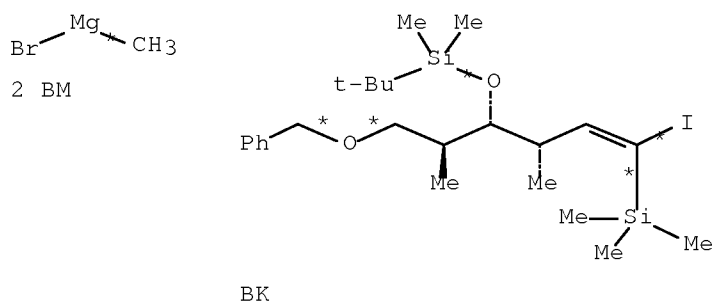
STAGE(3)
 RGT BO 7646-85-7 ZnCl2
 SOL 109-99-9 THF
 CON SUBSTAGE(1) 5 minutes, -78 deg C
 SUBSTAGE(2) 30 minutes, -78 deg C -> 0 deg C

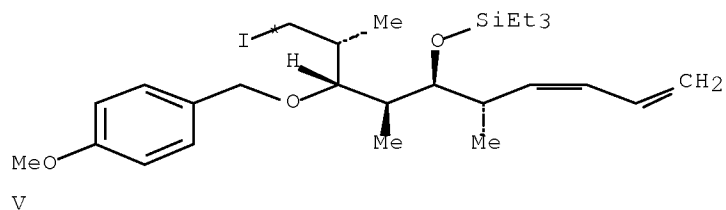
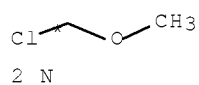
STAGE(4)
 RCT O 851889-66-2
 CAT 14221-01-3 Pd(PPh3)4
 SOL 109-99-9 THF
 CON SUBSTAGE(1) 1 hour, 0 deg C
 SUBSTAGE(2) 0 deg C -> room temperature
 SUBSTAGE(3) 6 hours, room temperature

STAGE(5)
 SOL 7732-18-5 Water
 CON room temperature

PRO DJ 851889-85-5
 NTE last stage quench

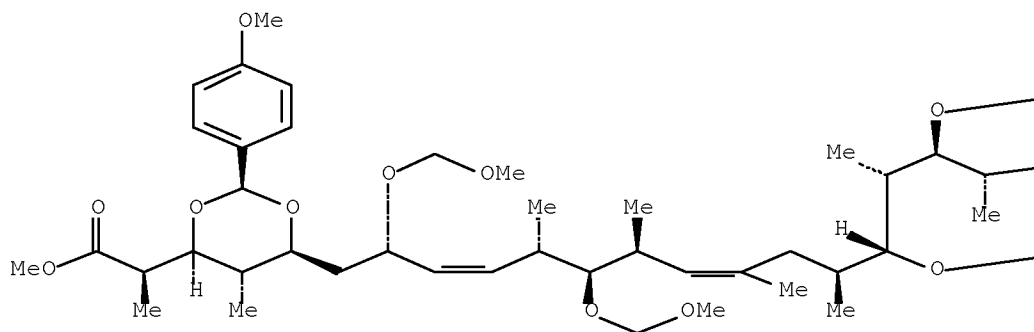
RX(503) OF 576 COMPOSED OF RX(15), RX(16), RX(17), RX(18), RX(6), RX(28),
 RX(29), RX(30), RX(31), RX(32), RX(33), RX(34), RX(3), RX(35)
 RX(503) 2 BM + 2 BK + BF + 2 AF + 2 AA + CM + CT + 2
 N + V ==> DJ





14
 STEPS


PAGE 1-A



* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

RX(15)

STAGE(1)

RGT BO 7646-85-7 ZnCl₂
 SOL 109-99-9 THF
 CON room temperature

STAGE(2)

RCT BM 75-16-1
 SOL 60-29-7 Et₂O
 CON 15 minutes, room temperature

STAGE(3)

RCT BK 444109-29-9
 CAT 14221-01-3 Pd(PPh₃)₄

SOL 109-99-9 THF
CON 2 hours, room temperature

STAGE(4)
RGT AI 12125-02-9 NH4Cl
SOL 7732-18-5 Water
CON room temperature

PRO BN 444109-30-2
NTE key step, stereoselective; last stage quench

RX(16)

STAGE(1)
RGT BS 1625-91-8 (p-t-BuC6H4)2
SOL 109-99-9 THF
CON room temperature

STAGE(2)
RGT BT 7439-93-2 Li
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) room temperature -> 25 deg C
SUBSTAGE(3) 5 hours, 15 - 25 deg C
SUBSTAGE(4) 15 deg C -> room temperature

STAGE(3)
RCT BN 444109-30-2
SOL 109-99-9 THF
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) 2.5 hours, -78 deg C

STAGE(4)
RGT AI 12125-02-9 NH4Cl
SOL 7732-18-5 Water
CON -78 deg C -> room temperature

PRO BR 444109-31-3
NTE first stage sonication; third stage inverse addn.; last stage quench

RX(17)

STAGE(1)
RGT AQ 79-37-8 (COCl)2
SOL 75-09-2 CH2Cl2
CON room temperature -> -78 deg C

STAGE(2)
RGT AP 67-68-5 DMSO
CON 45 minutes, -78 deg C

STAGE(3)
RCT BR 444109-31-3
SOL 75-09-2 CH2Cl2
CON 1 hour, -78 deg C

STAGE(4)
RGT AR 121-44-8 Et3N
CON SUBSTAGE(1) 15 minutes, -78 deg C
SUBSTAGE(2) 20 minutes, -78 deg C -> room temperature

PRO BU 444109-43-7
NTE last stage quench; Swern oxidn.

RX(18) RCT BF 558-13-4

STAGE(1)
RGT W 603-35-0 PPh3
SOL 75-09-2 CH2Cl2
CON 10 minutes, 0 deg C

STAGE(2)
RCT BU 444109-43-7
RGT BH 108-48-5 2,6-Lutidine
SOL 75-09-2 CH2Cl2
CON 4 hours, 0 deg C

STAGE(3)
RGT AI 12125-02-9 NH4Cl
SOL 7732-18-5 Water
CON 0 deg C

PRO AE 444109-32-4
NTE last stage quench; Corey-Fuchs olefination

RX(6) RCT AE 444109-32-4

STAGE(1)
SOL 109-99-9 THF
CON room temperature -> -78 deg C

STAGE(2)
RGT AH 109-72-8 BuLi
SOL 110-54-3 Hexane
CON SUBSTAGE(1) 30 minutes, -78 deg C
SUBSTAGE(2) -78 deg C -> -20 deg C
SUBSTAGE(3) 1 hour, -20 deg C
SUBSTAGE(4) -20 deg C -> -78 deg C

STAGE(3)
RCT AF 109-94-4
CON SUBSTAGE(1) 2 hours, -78 deg C
SUBSTAGE(2) -78 deg C -> 30 deg C
SUBSTAGE(3) 8 hours, 30 deg C

STAGE(4)
RGT AI 12125-02-9 NH4Cl
SOL 7732-18-5 Water
CON 30 deg C -> room temperature

PRO AG 444109-23-3
NTE last stage quench

RX(28) RCT AA 652986-45-3

STAGE(1)
SOL 75-09-2 CH2Cl2
CON room temperature -> -78 deg C

STAGE(2)

RGT R 7087-68-5 EtN(Pr-i)2
CON 5 minutes, -78 deg C

STAGE(3)

RGT CK 60669-69-4 F3CSO3BBu2
CON 45 minutes, -78 deg C

STAGE(4)

RCT AG 444109-23-3
SOL 75-09-2 CH2Cl2
CON 1 hour, -78 deg C

STAGE(5)

SOL 7732-18-5 Water, 67-56-1 MeOH
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> 0 deg C

STAGE(6)

RGT CL 7722-84-1 H2O2
SOL 7732-18-5 Water, 67-56-1 MeOH
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature

STAGE(7)

RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water
CON room temperature

PRO CJ 851889-73-1

NTE key step, stereoselective (d.r. 30:1); fifth stage phosphate
buffer; aldol reaction

RX(29) RCT CJ 851889-73-1

STAGE(1)

SOL 109-99-9 THF
CON room temperature

STAGE(2)

RCT CM 78-84-2
CON room temperature -> -10 deg C

STAGE(3)

RGT CO 32248-43-4 SmI2
SOL 109-99-9 THF
CON 4 hours, -10 deg C

STAGE(4)

RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water
CON -10 deg C -> room temperature

PRO CN 851889-75-3

NTE last stage quench

RX(30) RCT CN 851889-75-3

STAGE(1)

SOL 67-56-1 MeOH
CON room temperature

STAGE(2)
 RGT CR 1310-58-3 KOH
 CON room temperature

PRO CP 851889-76-4, CQ 851889-77-5
 NTE reaction monitored by TLC

RX(31) RCT CQ 851889-77-5
 PRO CP 851889-76-4
 CAT 24057-28-1 Pyridinium tosylate
 SOL 75-09-2 CH₂Cl₂
 NTE no reaction details

RX(32) RCT CP 851889-76-4

STAGE(1)
 SOL 71-43-2 Benzene
 CON room temperature

STAGE(2)
 CAT 15529-49-4 RuCl₂(PPh₃)₃
 CON 2 hours, room temperature

STAGE(3)
 CAT 15529-49-4 RuCl₂(PPh₃)₃
 CON 6 hours, room temperature

STAGE(4)
 RGT CV 513-35-9 Me₂C:CHMe
 SOL 75-65-0 t-BuOH
 CON room temperature

STAGE(5)
 RGT CW 7558-80-7 NaH₂PO₄, CX 7758-19-2 NaOClO
 SOL 7732-18-5 Water
 CON 1 hour, room temperature

STAGE(6)
 RGT CW 7558-80-7 NaH₂PO₄, CX 7758-19-2 NaOClO
 SOL 7732-18-5 Water
 CON 1 hour, room temperature

STAGE(7)
 SOL 60-29-7 Et₂O
 CON room temperature

STAGE(8)
 RGT C 7647-01-0 HCl
 SOL 7732-18-5 Water
 CON room temperature

STAGE(9)
 SOL 67-56-1 MeOH, 71-43-2 Benzene
 CON room temperature

STAGE(10)
 RCT CT 18107-18-1
 SOL 110-54-3 Hexane
 CON 15 minutes, room temperature

PRO CU 851889-79-7
NTE last stage acidification

RX(33) RCT CU 851889-79-7

STAGE(1)
RGT R 7087-68-5 EtN(Pr-i)2
SOL 75-09-2 CH2Cl2
CON room temperature -> 0 deg C

STAGE(2)
CAT 1122-58-3 4-DMAP
CON 0 deg C

STAGE(3)
RCT N 107-30-2
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 8 hours, 0 deg C -> room temperature

STAGE(4)
RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water

PRO DB 851889-80-0

RX(34) RCT DB 851889-80-0

STAGE(1)
SOL 110-54-3 Hexane
CON room temperature

STAGE(2)
CAT 91-22-5 Quinoline
CON room temperature

STAGE(3)
CAT 7440-05-3 Pd
CON room temperature

STAGE(4)
RGT DC 1333-74-0 H2
CON 8 hours, room temperature

STAGE(5)
SOL 107-14-2 ClCH2CN, 75-05-8 MeCN
CON room temperature

STAGE(6)
RGT DD 516-12-1 Iodosuccinimide
CON 3 hours, room temperature

STAGE(7)
RGT DE 7772-98-7 Na2S2O3
SOL 7732-18-5 Water
CON room temperature

PRO M 851889-82-2
NTE stereoselective; third stage Lindlar catalyst; sixth stage in dark; last stage quench

RX(3) RCT M 851889-82-2

STAGE(1)
SOL 109-99-9 THF
CON room temperature

STAGE(2)
RGT P 64-19-7 AcOH, Q 429-41-4 Bu4N.F
SOL 109-99-9 THF
CON 36 hours, room temperature

STAGE(3)
SOL 7732-18-5 Water
CON room temperature, pH 7

STAGE(4)
RGT R 7087-68-5 EtN(Pr-i)2
SOL 56-23-5 CCl4
CON room temperature -> 0 deg C

STAGE(5)
CAT 1122-58-3 4-DMAP
CON 0 deg C

STAGE(6)
RCT N 107-30-2
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 8 hours, 0 deg C -> room temperature

STAGE(7)
RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water

PRO O 851889-66-2
NTE third stage quench

RX(35) RCT V 216669-69-1

STAGE(1)
SOL 60-29-7 Et2O
CON room temperature -> -78 deg C

STAGE(2)
RGT DK 594-19-4 t-BuLi
SOL 109-66-0 Pentane
CON 30 minutes, -78 deg C

STAGE(3)
RGT BO 7646-85-7 ZnCl2
SOL 109-99-9 THF
CON SUBSTAGE(1) 5 minutes, -78 deg C
SUBSTAGE(2) 30 minutes, -78 deg C -> 0 deg C

STAGE(4)
RCT O 851889-66-2
CAT 14221-01-3 Pd(PPh3)4
SOL 109-99-9 THF
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature

SUBSTAGE(3) 6 hours, room temperature

STAGE(5)

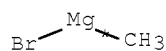
SOL 7732-18-5 Water

CON room temperature

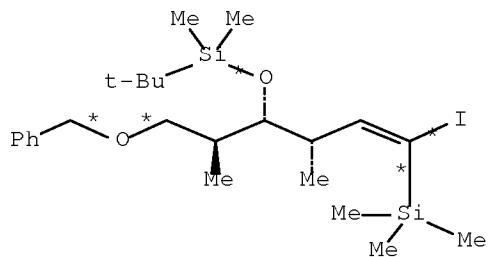
PRO DJ 851889-85-5

NTE last stage quench

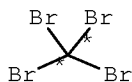
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RX(29), RX(30), RX(32), RX(33), RX(34), RX(3), RX(35), RX(36)
RX(504) BM + BK + BF + AF + AA + CM + CT + 2 N +
V ==> G



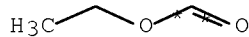
BM



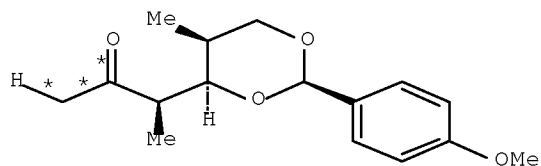
BK



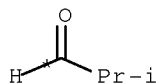
BF



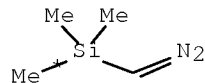
AF



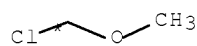
AA



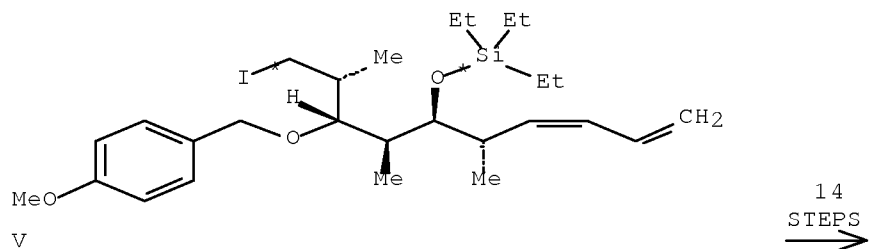
CM



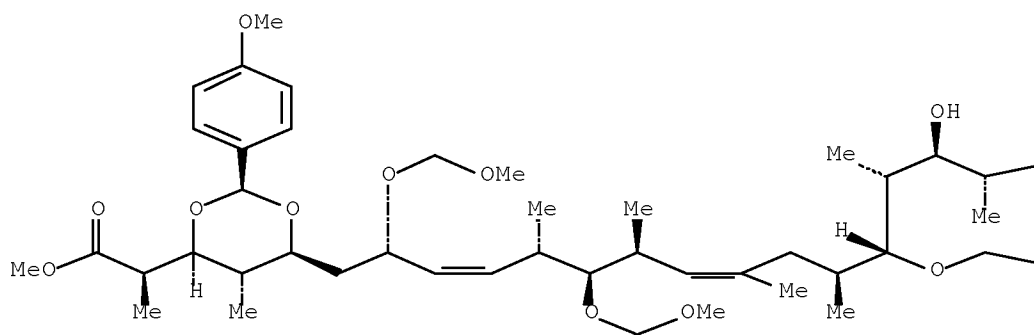
CT



2 N



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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

RX(15)

STAGE(1)

RGT BO 7646-85-7 ZnCl₂
 SOL 109-99-9 THF
 CON room temperature

STAGE(2)

RCT BM 75-16-1
 SOL 60-29-7 Et₂O
 CON 15 minutes, room temperature

STAGE(3)

RCT BK 444109-29-9
 CAT 14221-01-3 Pd(PPh₃)₄
 SOL 109-99-9 THF
 CON 2 hours, room temperature

STAGE(4)

RGT AI 12125-02-9 NH₄Cl
 SOL 7732-18-5 Water
 CON room temperature

PRO BN 444109-30-2

NTE key step, stereoselective; last stage quench

RX(16)

STAGE(1)

RGT BS 1625-91-8 (p-t-BuC6H4)2
SOL 109-99-9 THF
CON room temperature

STAGE(2)

RGT BT 7439-93-2 Li
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) room temperature -> 25 deg C
SUBSTAGE(3) 5 hours, 15 - 25 deg C
SUBSTAGE(4) 15 deg C -> room temperature

STAGE(3)

RCT BN 444109-30-2
SOL 109-99-9 THF
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) 2.5 hours, -78 deg C

STAGE(4)

RGT AI 12125-02-9 NH4Cl
SOL 7732-18-5 Water
CON -78 deg C -> room temperature

PRO BR 444109-31-3

NTE first stage sonication; third stage inverse addn.; last stage quench

RX(17)

STAGE(1)

RGT AQ 79-37-8 (COCl)2
SOL 75-09-2 CH2Cl2
CON room temperature -> -78 deg C

STAGE(2)

RGT AP 67-68-5 DMSO
CON 45 minutes, -78 deg C

STAGE(3)

RCT BR 444109-31-3
SOL 75-09-2 CH2Cl2
CON 1 hour, -78 deg C

STAGE(4)

RGT AR 121-44-8 Et3N
CON SUBSTAGE(1) 15 minutes, -78 deg C
SUBSTAGE(2) 20 minutes, -78 deg C -> room temperature

PRO BU 444109-43-7

NTE last stage quench; Swern oxidn.

RX(18)

RCT BF 558-13-4

STAGE(1)

RGT W 603-35-0 PPh3
SOL 75-09-2 CH2Cl2

CON 10 minutes, 0 deg C

STAGE(2)

RCT BU 444109-43-7
RGT BH 108-48-5 2,6-Lutidine
SOL 75-09-2 CH₂Cl₂
CON 4 hours, 0 deg C

STAGE(3)

RGT AI 12125-02-9 NH₄Cl
SOL 7732-18-5 Water
CON 0 deg C

PRO AE 444109-32-4

NTE last stage quench; Corey-Fuchs olefination

RX(6) RCT AE 444109-32-4

STAGE(1)

SOL 109-99-9 THF
CON room temperature -> -78 deg C

STAGE(2)

RGT AH 109-72-8 BuLi
SOL 110-54-3 Hexane
CON SUBSTAGE(1) 30 minutes, -78 deg C
SUBSTAGE(2) -78 deg C -> -20 deg C
SUBSTAGE(3) 1 hour, -20 deg C
SUBSTAGE(4) -20 deg C -> -78 deg C

STAGE(3)

RCT AF 109-94-4
CON SUBSTAGE(1) 2 hours, -78 deg C
SUBSTAGE(2) -78 deg C -> 30 deg C
SUBSTAGE(3) 8 hours, 30 deg C

STAGE(4)

RGT AI 12125-02-9 NH₄Cl
SOL 7732-18-5 Water
CON 30 deg C -> room temperature

PRO AG 444109-23-3

NTE last stage quench

RX(28) RCT AA 652986-45-3

STAGE(1)

SOL 75-09-2 CH₂Cl₂
CON room temperature -> -78 deg C

STAGE(2)

RGT R 7087-68-5 EtN(Pr-i)₂
CON 5 minutes, -78 deg C

STAGE(3)

RGT CK 60669-69-4 F₃CSO₃BBu₂
CON 45 minutes, -78 deg C

STAGE(4)

RCT AG 444109-23-3

SOL 75-09-2 CH₂Cl₂
CON 1 hour, -78 deg C

STAGE(5)

SOL 7732-18-5 Water, 67-56-1 MeOH
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> 0 deg C

STAGE(6)

RGT CL 7722-84-1 H₂O₂
SOL 7732-18-5 Water, 67-56-1 MeOH
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature

STAGE(7)

RGT D 144-55-8 NaHCO₃
SOL 7732-18-5 Water
CON room temperature

PRO CJ 851889-73-1

NTE key step, stereoselective (d.r. 30:1); fifth stage phosphate
buffer; aldol reaction

RX(29) RCT CJ 851889-73-1

STAGE(1)

SOL 109-99-9 THF
CON room temperature

STAGE(2)

RCT CM 78-84-2
CON room temperature -> -10 deg C

STAGE(3)

RGT CO 32248-43-4 SmI₂
SOL 109-99-9 THF
CON 4 hours, -10 deg C

STAGE(4)

RGT D 144-55-8 NaHCO₃
SOL 7732-18-5 Water
CON -10 deg C -> room temperature

PRO CN 851889-75-3

NTE last stage quench

RX(30) RCT CN 851889-75-3

STAGE(1)

SOL 67-56-1 MeOH
CON room temperature

STAGE(2)

RGT CR 1310-58-3 KOH
CON room temperature

PRO CP 851889-76-4, CQ 851889-77-5

NTE reaction monitored by TLC

RX(32) RCT CP 851889-76-4

STAGE(1)
SOL 71-43-2 Benzene
CON room temperature

STAGE(2)
CAT 15529-49-4 RuCl₂(PPh₃)₃
CON 2 hours, room temperature

STAGE(3)
CAT 15529-49-4 RuCl₂(PPh₃)₃
CON 6 hours, room temperature

STAGE(4)
RGT CV 513-35-9 Me₂C:CHMe
SOL 75-65-0 t-BuOH
CON room temperature

STAGE(5)
RGT CW 7558-80-7 NaH₂PO₄, CX 7758-19-2 NaOClO
SOL 7732-18-5 Water
CON 1 hour, room temperature

STAGE(6)
RGT CW 7558-80-7 NaH₂PO₄, CX 7758-19-2 NaOClO
SOL 7732-18-5 Water
CON 1 hour, room temperature

STAGE(7)
SOL 60-29-7 Et₂O
CON room temperature

STAGE(8)
RGT C 7647-01-0 HCl
SOL 7732-18-5 Water
CON room temperature

STAGE(9)
SOL 67-56-1 MeOH, 71-43-2 Benzene
CON room temperature

STAGE(10)
RCT CT 18107-18-1
SOL 110-54-3 Hexane
CON 15 minutes, room temperature

PRO CU 851889-79-7
NTE last stage acidification

RX(33) RCT CU 851889-79-7

STAGE(1)
RGT R 7087-68-5 EtN(Pr-i)₂
SOL 75-09-2 CH₂Cl₂
CON room temperature -> 0 deg C

STAGE(2)
CAT 1122-58-3 4-DMAP
CON 0 deg C


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STAGE(3)
  RCT  N 107-30-2
  CON  SUBSTAGE(1) 0 deg C
        SUBSTAGE(2) 8 hours, 0 deg C -> room temperature

STAGE(4)
  RGT  D 144-55-8 NaHCO3
  SOL  7732-18-5 Water

PRO   DB 851889-80-0

RX(34)  RCT  DB 851889-80-0

  STAGE(1)
    SOL  110-54-3 Hexane
    CON  room temperature

  STAGE(2)
    CAT  91-22-5 Quinoline
    CON  room temperature

  STAGE(3)
    CAT  7440-05-3 Pd
    CON  room temperature

  STAGE(4)
    RGT  DC 1333-74-0 H2
    CON  8 hours, room temperature

  STAGE(5)
    SOL  107-14-2 ClCH2CN, 75-05-8 MeCN
    CON  room temperature

  STAGE(6)
    RGT  DD 516-12-1 Iodosuccinimide
    CON  3 hours, room temperature

  STAGE(7)
    RGT  DE 7772-98-7 Na2S2O3
    SOL  7732-18-5 Water
    CON  room temperature

PRO   M 851889-82-2
NTE   stereoselective; third stage Lindlar catalyst; sixth stage in
      dark; last stage quench

RX(3)  RCT  M 851889-82-2

  STAGE(1)
    SOL  109-99-9 THF
    CON  room temperature

  STAGE(2)
    RGT  P 64-19-7 AcOH, Q 429-41-4 Bu4N.F
    SOL  109-99-9 THF
    CON  36 hours, room temperature

  STAGE(3)
    SOL  7732-18-5 Water
    CON  room temperature, pH 7

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STAGE(4)
  RGT  R 7087-68-5 EtN(Pr-i)2
  SOL  56-23-5 CCl4
  CON  room temperature -> 0 deg C

STAGE(5)
  CAT  1122-58-3 4-DMAP
  CON  0 deg C

STAGE(6)
  RCT  N 107-30-2
  CON  SUBSTAGE(1) 0 deg C
      SUBSTAGE(2) 8 hours, 0 deg C -> room temperature

STAGE(7)
  RGT  D 144-55-8 NaHCO3
  SOL  7732-18-5 Water

PRO  O 851889-66-2
NTE  third stage quench

RX(35)  RCT  V 216669-69-1

      STAGE(1)
        SOL  60-29-7 Et2O
        CON  room temperature -> -78 deg C

      STAGE(2)
        RGT  DK 594-19-4 t-BuLi
        SOL  109-66-0 Pentane
        CON  30 minutes, -78 deg C

      STAGE(3)
        RGT  BO 7646-85-7 ZnCl2
        SOL  109-99-9 THF
        CON  SUBSTAGE(1) 5 minutes, -78 deg C
            SUBSTAGE(2) 30 minutes, -78 deg C -> 0 deg C

      STAGE(4)
        RCT  O 851889-66-2
        CAT  14221-01-3 Pd(PPh3)4
        SOL  109-99-9 THF
        CON  SUBSTAGE(1) 1 hour, 0 deg C
            SUBSTAGE(2) 0 deg C -> room temperature
            SUBSTAGE(3) 6 hours, room temperature

      STAGE(5)
        SOL  7732-18-5 Water
        CON  room temperature

PRO  DJ 851889-85-5
NTE  last stage quench

RX(36)  RCT  DJ 851889-85-5

      STAGE(1)
        SOL  67-56-1 MeOH
        CON  room temperature -> 0 deg C

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STAGE(2)

CAT 104-15-4 TsOH

CON 1 hour, 0 deg C

STAGE(3)

RGT AR 121-44-8 Et3N

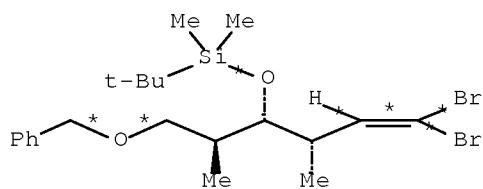
CON 0 deg C

PRO G 851889-86-6

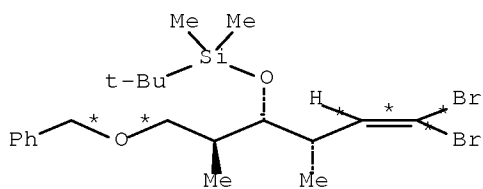
NTE last stage quench

RX(507) OF 576 COMPOSED OF RX(13), RX(14), RX(15), RX(16), RX(17), RX(18),
RX(6), RX(28), RX(29), RX(30), RX(31), RX(32), RX(33), RX(34), RX(3),
RX(35)

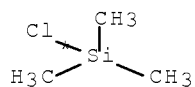
RX(507) 2 BG + 2 BI + 2 BM + BF + 2 AF + 2 AA + CM +
CT + 2 N + V ==> DJ



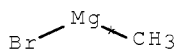
BG



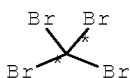
BG



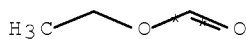
2 BI



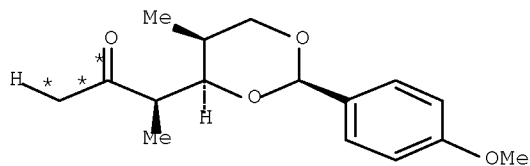
2 BM



BF



2 AF



AA



STEPS
→

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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

RX(13) RCT BG 444109--27--7

STAGE (1)

SOL 109-99-9 THF

CON room temperature -> -78 deg C

STAGE(2)

RGT AH 109-72-8 BuLi
SOL 110-54-3 Hexane
CON SUBSTAGE(1) 1 hour, -78 deg C
SUBSTAGE(2) -78 deg C -> -20 deg C
SUBSTAGE(3) 1 hour, -20 deg C
SUBSTAGE(4) -20 deg C -> -78 deg C

STAGE(3)

RCT BI 75-77-4
CON 8 hours, -78 deg C -> room temperature

STAGE(4)

RGT AI 12125-02-9 NH4Cl
SOL 7732-18-5 Water

PRO BJ 444109-28-8

RX(14) RCT BJ 444109-28-8

STAGE(1)

SOL 109-99-9 THF
CON room temperature

STAGE(2)

RGT BL 37342-97-5 Hydrozirconocene Cl
CON SUBSTAGE(1) 5 minutes, room temperature
SUBSTAGE(2) room temperature -> 55 deg C
SUBSTAGE(3) 1 hour, 55 deg C
SUBSTAGE(4) 55 deg C -> room temperature

STAGE(3)

RGT X 7553-56-2 I2
SOL 109-99-9 THF
CON 20 minutes, room temperature

PRO BK 444109-29-9

RX(15)

STAGE(1)

RGT BO 7646-85-7 ZnCl2
SOL 109-99-9 THF
CON room temperature

STAGE(2)

RCT BM 75-16-1
SOL 60-29-7 Et2O
CON 15 minutes, room temperature

STAGE(3)

RCT BK 444109-29-9
CAT 14221-01-3 Pd(PPh3)4
SOL 109-99-9 THF
CON 2 hours, room temperature

STAGE(4)

RGT AI 12125-02-9 NH4Cl
SOL 7732-18-5 Water

CON room temperature

PRO BN 444109-30-2

NTE key step, stereoselective; last stage quench

RX(16)

STAGE(1)

RGT BS 1625-91-8 (p-t-BuC₆H₄)₂

SOL 109-99-9 THF

CON room temperature

STAGE(2)

RGT BT 7439-93-2 Li

CON SUBSTAGE(1) room temperature

SUBSTAGE(2) room temperature -> 25 deg C

SUBSTAGE(3) 5 hours, 15 - 25 deg C

SUBSTAGE(4) 15 deg C -> room temperature

STAGE(3)

RCT BN 444109-30-2

SOL 109-99-9 THF

CON SUBSTAGE(1) room temperature -> -78 deg C

SUBSTAGE(2) 2.5 hours, -78 deg C

STAGE(4)

RGT AI 12125-02-9 NH₄Cl

SOL 7732-18-5 Water

CON -78 deg C -> room temperature

PRO BR 444109-31-3

NTE first stage sonication; third stage inverse addn.; last stage quench

RX(17)

STAGE(1)

RGT AQ 79-37-8 (COCl)₂

SOL 75-09-2 CH₂Cl₂

CON room temperature -> -78 deg C

STAGE(2)

RGT AP 67-68-5 DMSO

CON 45 minutes, -78 deg C

STAGE(3)

RCT BR 444109-31-3

SOL 75-09-2 CH₂Cl₂

CON 1 hour, -78 deg C

STAGE(4)

RGT AR 121-44-8 Et₃N

CON SUBSTAGE(1) 15 minutes, -78 deg C

SUBSTAGE(2) 20 minutes, -78 deg C -> room temperature

PRO BU 444109-43-7

NTE last stage quench; Swern oxidn.

RX(18)

RCT BF 558-13-4

STAGE(1)
RGT W 603-35-0 PPh3
SOL 75-09-2 CH2Cl2
CON 10 minutes, 0 deg C

STAGE(2)
RCT BU 444109-43-7
RGT BH 108-48-5 2,6-Lutidine
SOL 75-09-2 CH2Cl2
CON 4 hours, 0 deg C

STAGE(3)
RGT AI 12125-02-9 NH4Cl
SOL 7732-18-5 Water
CON 0 deg C

PRO AE 444109-32-4
NTE last stage quench; Corey-Fuchs olefination

RX(6) RCT AE 444109-32-4

STAGE(1)
SOL 109-99-9 THF
CON room temperature -> -78 deg C

STAGE(2)
RGT AH 109-72-8 BuLi
SOL 110-54-3 Hexane
CON SUBSTAGE(1) 30 minutes, -78 deg C
SUBSTAGE(2) -78 deg C -> -20 deg C
SUBSTAGE(3) 1 hour, -20 deg C
SUBSTAGE(4) -20 deg C -> -78 deg C

STAGE(3)
RCT AF 109-94-4
CON SUBSTAGE(1) 2 hours, -78 deg C
SUBSTAGE(2) -78 deg C -> 30 deg C
SUBSTAGE(3) 8 hours, 30 deg C

STAGE(4)
RGT AI 12125-02-9 NH4Cl
SOL 7732-18-5 Water
CON 30 deg C -> room temperature

PRO AG 444109-23-3
NTE last stage quench

RX(28) RCT AA 652986-45-3

STAGE(1)
SOL 75-09-2 CH2Cl2
CON room temperature -> -78 deg C

STAGE(2)
RGT R 7087-68-5 EtN(Pr-i)2
CON 5 minutes, -78 deg C

STAGE(3)
RGT CK 60669-69-4 F3CSO3BBu2
CON 45 minutes, -78 deg C

STAGE(4)
RCT AG 444109-23-3
SOL 75-09-2 CH2Cl2
CON 1 hour, -78 deg C

STAGE(5)
SOL 7732-18-5 Water, 67-56-1 MeOH
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> 0 deg C

STAGE(6)
RGT CL 7722-84-1 H2O2
SOL 7732-18-5 Water, 67-56-1 MeOH
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature

STAGE(7)
RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water
CON room temperature

PRO CJ 851889-73-1
NTE key step, stereoselective (d.r. 30:1); fifth stage phosphate
buffer; aldol reaction

RX(29) RCT CJ 851889-73-1

STAGE(1)
SOL 109-99-9 THF
CON room temperature

STAGE(2)
RCT CM 78-84-2
CON room temperature -> -10 deg C

STAGE(3)
RGT CO 32248-43-4 SmI2
SOL 109-99-9 THF
CON 4 hours, -10 deg C

STAGE(4)
RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water
CON -10 deg C -> room temperature

PRO CN 851889-75-3
NTE last stage quench

RX(30) RCT CN 851889-75-3

STAGE(1)
SOL 67-56-1 MeOH
CON room temperature

STAGE(2)
RGT CR 1310-58-3 KOH
CON room temperature

PRO CP 851889-76-4, CQ 851889-77-5

NTE reaction monitored by TLC

RX(31) RCT CQ 851889-77-5
PRO CP 851889-76-4
CAT 24057-28-1 Pyridinium tosylate
SOL 75-09-2 CH₂Cl₂
NTE no reaction details

RX(32) RCT CP 851889-76-4

STAGE(1)

SOL 71-43-2 Benzene
CON room temperature

STAGE(2)

CAT 15529-49-4 RuCl₂(PPh₃)₃
CON 2 hours, room temperature

STAGE(3)

CAT 15529-49-4 RuCl₂(PPh₃)₃
CON 6 hours, room temperature

STAGE(4)

RGT CV 513-35-9 Me₂C:CHMe
SOL 75-65-0 t-BuOH
CON room temperature

STAGE(5)

RGT CW 7558-80-7 NaH₂PO₄, CX 7758-19-2 NaOClO
SOL 7732-18-5 Water
CON 1 hour, room temperature

STAGE(6)

RGT CW 7558-80-7 NaH₂PO₄, CX 7758-19-2 NaOClO
SOL 7732-18-5 Water
CON 1 hour, room temperature

STAGE(7)

SOL 60-29-7 Et₂O
CON room temperature

STAGE(8)

RGT C 7647-01-0 HCl
SOL 7732-18-5 Water
CON room temperature

STAGE(9)

SOL 67-56-1 MeOH, 71-43-2 Benzene
CON room temperature

STAGE(10)

RCT CT 18107-18-1
SOL 110-54-3 Hexane
CON 15 minutes, room temperature

PRO CU 851889-79-7

NTE last stage acidification

RX(33) RCT CU 851889-79-7

```

STAGE(1)
  RGT  R 7087-68-5 EtN(Pr-i)2
  SOL  75-09-2 CH2Cl2
  CON  room temperature -> 0 deg C

STAGE(2)
  CAT  1122-58-3 4-DMAP
  CON  0 deg C

STAGE(3)
  RCT  N 107-30-2
  CON  SUBSTAGE(1) 0 deg C
      SUBSTAGE(2) 8 hours, 0 deg C -> room temperature

STAGE(4)
  RGT  D 144-55-8 NaHCO3
  SOL  7732-18-5 Water

PRO   DB 851889-80-0

RX(34)  RCT  DB 851889-80-0

  STAGE(1)
    SOL  110-54-3 Hexane
    CON  room temperature

  STAGE(2)
    CAT  91-22-5 Quinoline
    CON  room temperature

  STAGE(3)
    CAT  7440-05-3 Pd
    CON  room temperature

  STAGE(4)
    RGT  DC 1333-74-0 H2
    CON  8 hours, room temperature

  STAGE(5)
    SOL  107-14-2 ClCH2CN, 75-05-8 MeCN
    CON  room temperature

  STAGE(6)
    RGT  DD 516-12-1 Iodosuccinimide
    CON  3 hours, room temperature

  STAGE(7)
    RGT  DE 7772-98-7 Na2S2O3
    SOL  7732-18-5 Water
    CON  room temperature

PRO   M 851889-82-2
NTE   stereoselective; third stage Lindlar catalyst; sixth stage in
      dark; last stage quench

RX(3)  RCT  M 851889-82-2

  STAGE(1)
    SOL  109-99-9 THF
    CON  room temperature

```

STAGE(2)
 RGT P 64-19-7 AcOH, Q 429-41-4 Bu4N.F
 SOL 109-99-9 THF
 CON 36 hours, room temperature

STAGE(3)
 SOL 7732-18-5 Water
 CON room temperature, pH 7

STAGE(4)
 RGT R 7087-68-5 EtN(Pr-i)2
 SOL 56-23-5 CCl4
 CON room temperature -> 0 deg C

STAGE(5)
 CAT 1122-58-3 4-DMAP
 CON 0 deg C

STAGE(6)
 RCT N 107-30-2
 CON SUBSTAGE(1) 0 deg C
 SUBSTAGE(2) 8 hours, 0 deg C -> room temperature

STAGE(7)
 RGT D 144-55-8 NaHCO3
 SOL 7732-18-5 Water

PRO O 851889-66-2
 NTE third stage quench

RX(35) RCT V ~~216669-69-1~~

STAGE(1)
 SOL 60-29-7 Et2O
 CON room temperature -> -78 deg C

STAGE(2)
 RGT DK 594-19-4 t-BuLi
 SOL 109-66-0 Pentane
 CON 30 minutes, -78 deg C

STAGE(3)
 RGT BO 7646-85-7 ZnCl2
 SOL 109-99-9 THF
 CON SUBSTAGE(1) 5 minutes, -78 deg C
 SUBSTAGE(2) 30 minutes, -78 deg C -> 0 deg C

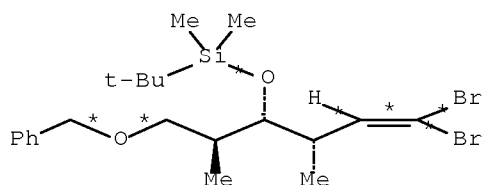
STAGE(4)
 RCT O 851889-66-2
 CAT 14221-01-3 Pd(PPh3)4
 SOL 109-99-9 THF
 CON SUBSTAGE(1) 1 hour, 0 deg C
 SUBSTAGE(2) 0 deg C -> room temperature
 SUBSTAGE(3) 6 hours, room temperature

STAGE(5)
 SOL 7732-18-5 Water
 CON room temperature

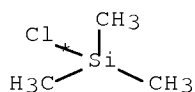
PRO DJ 851889--85--5
 NTE last stage quench

RX(508) OF 576 COMPOSED OF RX(13), RX(14), RX(15), RX(16), RX(17), RX(18),
 RX(6), RX(28), RX(29), RX(30), RX(32), RX(33), RX(34), RX(3), RX(35),
 RX(36)

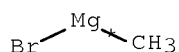
RX(508) BG + BI + BM + BF + AF + AA + CM + CT + 2 N
 + V ==> G



BG



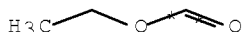
BI



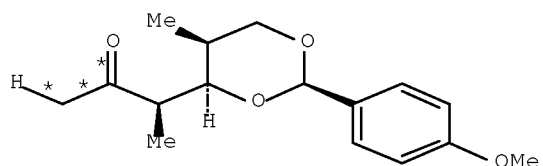
BM



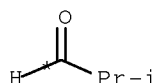
BF



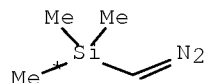
AF



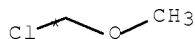
AA



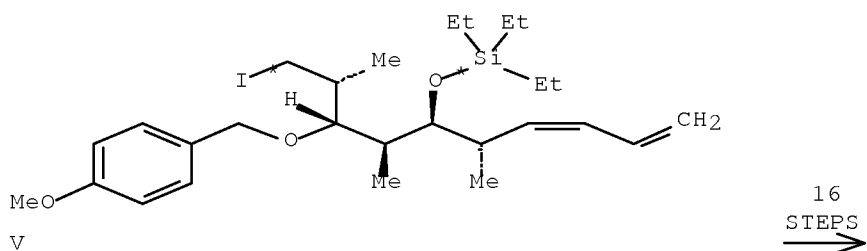
CM



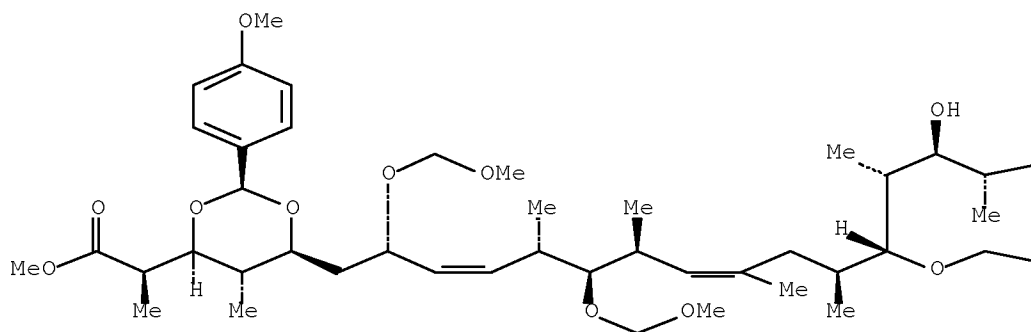
CT



2 N



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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

RX(13) RCT BG 444109-27-7

STAGE(1)

SOL 109-99-9 THF
CON room temperature -> -78 deg C

STAGE(2)

RGT AH 109-72-8 BuLi
SOL 110-54-3 Hexane
CON SUBSTAGE(1) 1 hour, -78 deg C
SUBSTAGE(2) -78 deg C -> -20 deg C
SUBSTAGE(3) 1 hour, -20 deg C
SUBSTAGE(4) -20 deg C -> -78 deg C

STAGE(3)

RCT BI 75-77-4
CON 8 hours, -78 deg C -> room temperature

STAGE(4)

RGT AI 12125-02-9 NH4Cl
SOL 7732-18-5 Water

PRO BJ 444109-28-8

RX(14) RCT BJ 444109-28-8

STAGE(1)
SOL 109-99-9 THF
CON room temperature

STAGE(2)
RGT BL 37342-97-5 Hydrozirconocene Cl
CON SUBSTAGE(1) 5 minutes, room temperature
SUBSTAGE(2) room temperature -> 55 deg C
SUBSTAGE(3) 1 hour, 55 deg C
SUBSTAGE(4) 55 deg C -> room temperature

STAGE(3)
RGT X 7553-56-2 I2
SOL 109-99-9 THF
CON 20 minutes, room temperature

PRO BK 444109-29-9

RX(15)

STAGE(1)
RGT BO 7646-85-7 ZnCl2
SOL 109-99-9 THF
CON room temperature

STAGE(2)
RCT BM 75-16-1
SOL 60-29-7 Et2O
CON 15 minutes, room temperature

STAGE(3)
RCT BK 444109-29-9
CAT 14221-01-3 Pd(PPh3)4
SOL 109-99-9 THF
CON 2 hours, room temperature

STAGE(4)
RGT AI 12125-02-9 NH4Cl
SOL 7732-18-5 Water
CON room temperature

PRO BN 444109-30-2
NTE key step, stereoselective; last stage quench

RX(16)

STAGE(1)
RGT BS 1625-91-8 (p-t-BuC6H4)2
SOL 109-99-9 THF
CON room temperature

STAGE(2)
RGT BT 7439-93-2 Li
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) room temperature -> 25 deg C
SUBSTAGE(3) 5 hours, 15 - 25 deg C
SUBSTAGE(4) 15 deg C -> room temperature

STAGE(3)

RCT BN 444109-30-2
SOL 109-99-9 THF
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) 2.5 hours, -78 deg C

STAGE(4)
RGT AI 12125-02-9 NH4Cl
SOL 7732-18-5 Water
CON -78 deg C -> room temperature

PRO BR 444109-31-3
NTE first stage sonication; third stage inverse addn.; last stage
quench

RX(17)

STAGE(1)
RGT AQ 79-37-8 (COCl)₂
SOL 75-09-2 CH₂Cl₂
CON room temperature -> -78 deg C

STAGE(2)
RGT AP 67-68-5 DMSO
CON 45 minutes, -78 deg C

STAGE(3)
RCT BR 444109-31-3
SOL 75-09-2 CH₂Cl₂
CON 1 hour, -78 deg C

STAGE(4)
RGT AR 121-44-8 Et₃N
CON SUBSTAGE(1) 15 minutes, -78 deg C
SUBSTAGE(2) 20 minutes, -78 deg C -> room temperature

PRO BU 444109-43-7
NTE last stage quench; Swern oxidn.

RX(18) RCT BF 558-13-4

STAGE(1)
RGT W 603-35-0 PPh₃
SOL 75-09-2 CH₂Cl₂
CON 10 minutes, 0 deg C

STAGE(2)
RCT BU 444109-43-7
RGT BH 108-48-5 2,6-Lutidine
SOL 75-09-2 CH₂Cl₂
CON 4 hours, 0 deg C

STAGE(3)
RGT AI 12125-02-9 NH₄Cl
SOL 7732-18-5 Water
CON 0 deg C

PRO AE 444109-32-4
NTE last stage quench; Corey-Fuchs olefination

RX(6) RCT AE 444109-32-4

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STAGE(1)
  SOL  109-99-9 THF
  CON  room temperature -> -78 deg C

STAGE(2)
  RGT  AH 109-72-8 BuLi
  SOL  110-54-3 Hexane
  CON  SUBSTAGE(1) 30 minutes, -78 deg C
      SUBSTAGE(2) -78 deg C -> -20 deg C
      SUBSTAGE(3) 1 hour, -20 deg C
      SUBSTAGE(4) -20 deg C -> -78 deg C

STAGE(3)
  RCT  AF 109-94-4
  CON  SUBSTAGE(1) 2 hours, -78 deg C
      SUBSTAGE(2) -78 deg C -> 30 deg C
      SUBSTAGE(3) 8 hours, 30 deg C

STAGE(4)
  RGT  AI 12125-02-9 NH4Cl
  SOL  7732-18-5 Water
  CON  30 deg C -> room temperature

PRO  AG 444109-23-3
NTE  last stage quench

RX(28)  RCT  AA 652986-45-3

STAGE(1)
  SOL  75-09-2 CH2Cl2
  CON  room temperature -> -78 deg C

STAGE(2)
  RGT  R 7087-68-5 EtN(Pr-i)2
  CON  5 minutes, -78 deg C

STAGE(3)
  RGT  CK 60669-69-4 F3CSO3BBu2
  CON  45 minutes, -78 deg C

STAGE(4)
  RCT  AG 444109-23-3
  SOL  75-09-2 CH2Cl2
  CON  1 hour, -78 deg C

STAGE(5)
  SOL  7732-18-5 Water, 67-56-1 MeOH
  CON  SUBSTAGE(1) -78 deg C
      SUBSTAGE(2) -78 deg C -> 0 deg C

STAGE(6)
  RGT  CL 7722-84-1 H2O2
  SOL  7732-18-5 Water, 67-56-1 MeOH
  CON  SUBSTAGE(1) 1 hour, 0 deg C
      SUBSTAGE(2) 0 deg C -> room temperature

STAGE(7)
  RGT  D 144-55-8 NaHCO3
  SOL  7732-18-5 Water

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        CON  room temperature

PRO  CJ 851889-73-1
NTE  key step, stereoselective (d.r. 30:1); fifth stage phosphate
      buffer; aldol reaction

RX(29)  RCT  CJ 851889-73-1

        STAGE(1)
          SOL  109-99-9 THF
          CON  room temperature

        STAGE(2)
          RCT  CM 78-84-2
          CON  room temperature -> -10 deg C

        STAGE(3)
          RGT  CO 32248-43-4 SmI2
          SOL  109-99-9 THF
          CON  4 hours, -10 deg C

        STAGE(4)
          RGT  D 144-55-8 NaHCO3
          SOL  7732-18-5 Water
          CON  -10 deg C -> room temperature

PRO  CN 851889-75-3
NTE  last stage quench

RX(30)  RCT  CN 851889-75-3

        STAGE(1)
          SOL  67-56-1 MeOH
          CON  room temperature

        STAGE(2)
          RGT  CR 1310-58-3 KOH
          CON  room temperature

PRO  CP 851889-76-4, CQ 851889-77-5
NTE  reaction monitored by TLC

RX(32)  RCT  CP 851889-76-4

        STAGE(1)
          SOL  71-43-2 Benzene
          CON  room temperature

        STAGE(2)
          CAT  15529-49-4 RuCl2(PPh3)3
          CON  2 hours, room temperature

        STAGE(3)
          CAT  15529-49-4 RuCl2(PPh3)3
          CON  6 hours, room temperature

        STAGE(4)
          RGT  CV 513-35-9 Me2C:CHMe
          SOL  75-65-0 t-BuOH
          CON  room temperature

```

STAGE(5)
RGT CW 7558-80-7 NaH2PO4, CX 7758-19-2 NaOClO
SOL 7732-18-5 Water
CON 1 hour, room temperature

STAGE(6)
RGT CW 7558-80-7 NaH2PO4, CX 7758-19-2 NaOClO
SOL 7732-18-5 Water
CON 1 hour, room temperature

STAGE(7)
SOL 60-29-7 Et2O
CON room temperature

STAGE(8)
RGT C 7647-01-0 HCl
SOL 7732-18-5 Water
CON room temperature

STAGE(9)
SOL 67-56-1 MeOH, 71-43-2 Benzene
CON room temperature

STAGE(10)
RCT CT 18107-18-1
SOL 110-54-3 Hexane
CON 15 minutes, room temperature

PRO CU 851889-79-7
NTE last stage acidification

RX(33) RCT CU 851889-79-7

STAGE(1)
RGT R 7087-68-5 EtN(Pr-i)2
SOL 75-09-2 CH2Cl2
CON room temperature -> 0 deg C

STAGE(2)
CAT 1122-58-3 4-DMAP
CON 0 deg C

STAGE(3)
RCT N 107-30-2
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 8 hours, 0 deg C -> room temperature

STAGE(4)
RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water

PRO DB 851889-80-0

RX(34) RCT DB 851889-80-0

STAGE(1)
SOL 110-54-3 Hexane
CON room temperature

STAGE(2)
CAT 91-22-5 Quinoline
CON room temperature

STAGE(3)
CAT 7440-05-3 Pd
CON room temperature

STAGE(4)
RGT DC 1333-74-0 H2
CON 8 hours, room temperature

STAGE(5)
SOL 107-14-2 ClCH2CN, 75-05-8 MeCN
CON room temperature

STAGE(6)
RGT DD 516-12-1 Iodosuccinimide
CON 3 hours, room temperature

STAGE(7)
RGT DE 7772-98-7 Na2S2O3
SOL 7732-18-5 Water
CON room temperature

PRO M 851889-82-2
NTE stereoselective; third stage Lindlar catalyst; sixth stage in
dark; last stage quench

RX(3) RCT M 851889-82-2

STAGE(1)
SOL 109-99-9 THF
CON room temperature

STAGE(2)
RGT P 64-19-7 AcOH, Q 429-41-4 Bu4N.F
SOL 109-99-9 THF
CON 36 hours, room temperature

STAGE(3)
SOL 7732-18-5 Water
CON room temperature, pH 7

STAGE(4)
RGT R 7087-68-5 EtN(Pr-i)2
SOL 56-23-5 CCl4
CON room temperature -> 0 deg C

STAGE(5)
CAT 1122-58-3 4-DMAP
CON 0 deg C

STAGE(6)
RCT N 107-30-2
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 8 hours, 0 deg C -> room temperature

STAGE(7)
RGT D 144-55-8 NaHCO3

SOL 7732-18-5 Water

PRO O 851889-66-2
NTE third stage quench

RX(35) RCT V 216669-69-1

STAGE(1)
SOL 60-29-7 Et2O
CON room temperature -> -78 deg C

STAGE(2)
RGT DK 594-19-4 t-BuLi
SOL 109-66-0 Pentane
CON 30 minutes, -78 deg C

STAGE(3)
RGT BO 7646-85-7 ZnCl2
SOL 109-99-9 THF
CON SUBSTAGE(1) 5 minutes, -78 deg C
SUBSTAGE(2) 30 minutes, -78 deg C -> 0 deg C

STAGE(4)
RCT O 851889-66-2
CAT 14221-01-3 Pd(PPh3)4
SOL 109-99-9 THF
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature
SUBSTAGE(3) 6 hours, room temperature

STAGE(5)
SOL 7732-18-5 Water
CON room temperature

PRO DJ 851889-85-5
NTE last stage quench

RX(36) RCT DJ 851889-85-5

STAGE(1)
SOL 67-56-1 MeOH
CON room temperature -> 0 deg C

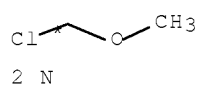
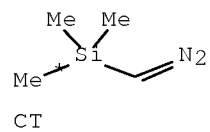
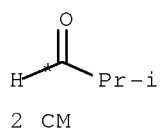
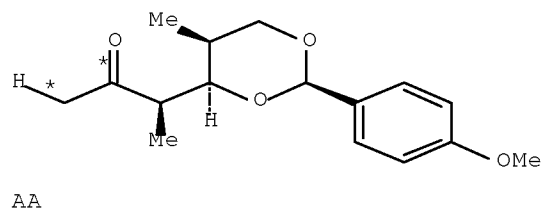
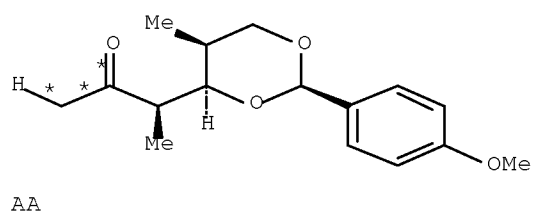
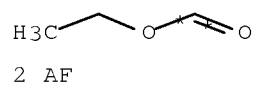
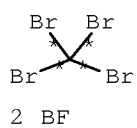
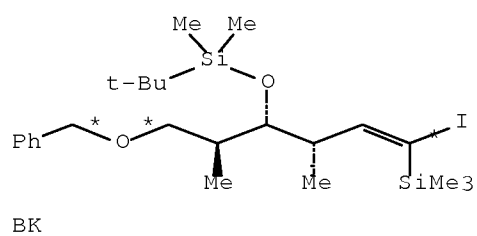
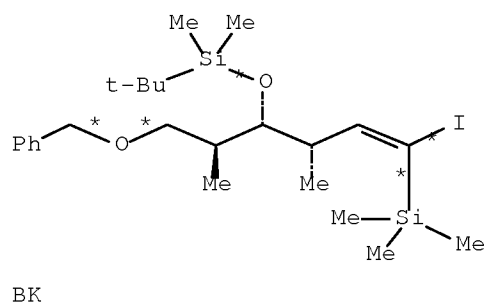
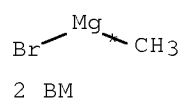
STAGE(2)
CAT 104-15-4 TsOH
CON 1 hour, 0 deg C

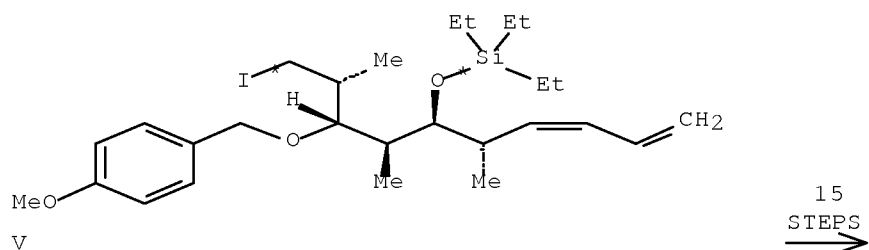
STAGE(3)
RGT AR 121-44-8 Et3N
CON 0 deg C

PRO G 851889-86-6
NTE last stage quench

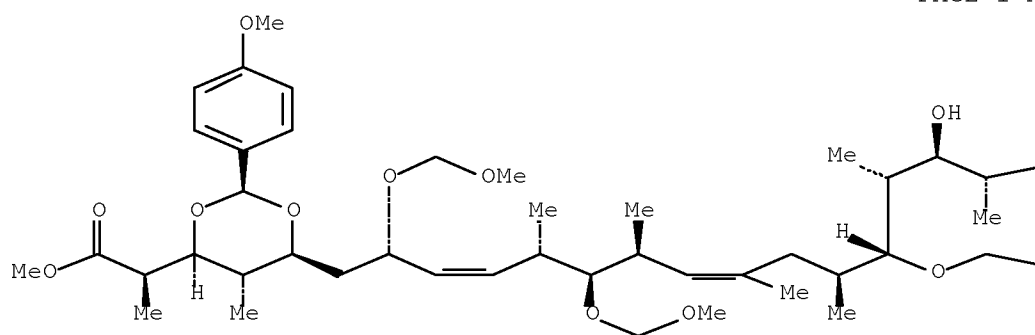
RX(529) OF 576 COMPOSED OF RX(15), RX(16), RX(17), RX(18), RX(6), RX(28),
RX(29), RX(30), RX(31), RX(32), RX(33), RX(34), RX(3), RX(35), RX(36)

RX(529) 2 BM + 2 BK + 2 BF + 2 AF + 2 AA + 2 CM + CT +
2 N + V ==> G





PAGE 1-A



* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

RX(15)

STAGE(1)

RGT BO 7646-85-7 ZnCl₂
 SOL 109-99-9 THF
 CON room temperature

STAGE(2)

RCT BM 75-16-1
 SOL 60-29-7 Et₂O
 CON 15 minutes, room temperature

STAGE(3)

RCT BK 444109-29-9
 CAT 14221-01-3 Pd(PPh₃)₄
 SOL 109-99-9 THF
 CON 2 hours, room temperature

STAGE(4)

RGT AI 12125-02-9 NH₄Cl
 SOL 7732-18-5 Water

CON room temperature

PRO BN 444109-30-2

NTE key step, stereoselective; last stage quench

RX(16)

STAGE(1)

RGT BS 1625-91-8 (p-t-BuC6H4)2

SOL 109-99-9 THF

CON room temperature

STAGE(2)

RGT BT 7439-93-2 Li

CON SUBSTAGE(1) room temperature

SUBSTAGE(2) room temperature -> 25 deg C

SUBSTAGE(3) 5 hours, 15 - 25 deg C

SUBSTAGE(4) 15 deg C -> room temperature

STAGE(3)

RCT BN 444109-30-2

SOL 109-99-9 THF

CON SUBSTAGE(1) room temperature -> -78 deg C

SUBSTAGE(2) 2.5 hours, -78 deg C

STAGE(4)

RGT AI 12125-02-9 NH4Cl

SOL 7732-18-5 Water

CON -78 deg C -> room temperature

PRO BR 444109-31-3

NTE first stage sonication; third stage inverse addn.; last stage quench

RX(17)

STAGE(1)

RGT AQ 79-37-8 (COCl)2

SOL 75-09-2 CH2Cl2

CON room temperature -> -78 deg C

STAGE(2)

RGT AP 67-68-5 DMSO

CON 45 minutes, -78 deg C

STAGE(3)

RCT BR 444109-31-3

SOL 75-09-2 CH2Cl2

CON 1 hour, -78 deg C

STAGE(4)

RGT AR 121-44-8 Et3N

CON SUBSTAGE(1) 15 minutes, -78 deg C

SUBSTAGE(2) 20 minutes, -78 deg C -> room temperature

PRO BU 444109-43-7

NTE last stage quench; Swern oxidn.

RX(18)

RCT BF 558-13-4

STAGE(1)
RGT W 603-35-0 PPh3
SOL 75-09-2 CH2Cl2
CON 10 minutes, 0 deg C

STAGE(2)
RCT BU 444109-43-7
RGT BH 108-48-5 2,6-Lutidine
SOL 75-09-2 CH2Cl2
CON 4 hours, 0 deg C

STAGE(3)
RGT AI 12125-02-9 NH4Cl
SOL 7732-18-5 Water
CON 0 deg C

PRO AE 444109-32-4
NTE last stage quench; Corey-Fuchs olefination

RX(6) RCT AE 444109-32-4

STAGE(1)
SOL 109-99-9 THF
CON room temperature -> -78 deg C

STAGE(2)
RGT AH 109-72-8 BuLi
SOL 110-54-3 Hexane
CON SUBSTAGE(1) 30 minutes, -78 deg C
SUBSTAGE(2) -78 deg C -> -20 deg C
SUBSTAGE(3) 1 hour, -20 deg C
SUBSTAGE(4) -20 deg C -> -78 deg C

STAGE(3)
RCT AF 109-94-4
CON SUBSTAGE(1) 2 hours, -78 deg C
SUBSTAGE(2) -78 deg C -> 30 deg C
SUBSTAGE(3) 8 hours, 30 deg C

STAGE(4)
RGT AI 12125-02-9 NH4Cl
SOL 7732-18-5 Water
CON 30 deg C -> room temperature

PRO AG 444109-23-3
NTE last stage quench

RX(28) RCT AA 652986-45-3

STAGE(1)
SOL 75-09-2 CH2Cl2
CON room temperature -> -78 deg C

STAGE(2)
RGT R 7087-68-5 EtN(Pr-i)2
CON 5 minutes, -78 deg C

STAGE(3)
RGT CK 60669-69-4 F3CSO3BBu2
CON 45 minutes, -78 deg C

STAGE(4)
RCT AG 444109-23-3
SOL 75-09-2 CH2Cl2
CON 1 hour, -78 deg C

STAGE(5)
SOL 7732-18-5 Water, 67-56-1 MeOH
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> 0 deg C

STAGE(6)
RGT CL 7722-84-1 H2O2
SOL 7732-18-5 Water, 67-56-1 MeOH
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature

STAGE(7)
RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water
CON room temperature

PRO CJ 851889-73-1
NTE key step, stereoselective (d.r. 30:1); fifth stage phosphate
buffer; aldol reaction

RX(29) RCT CJ 851889-73-1

STAGE(1)
SOL 109-99-9 THF
CON room temperature

STAGE(2)
RCT CM 78-84-2
CON room temperature -> -10 deg C

STAGE(3)
RGT CO 32248-43-4 SmI2
SOL 109-99-9 THF
CON 4 hours, -10 deg C

STAGE(4)
RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water
CON -10 deg C -> room temperature

PRO CN 851889-75-3
NTE last stage quench

RX(30) RCT CN 851889-75-3

STAGE(1)
SOL 67-56-1 MeOH
CON room temperature

STAGE(2)
RGT CR 1310-58-3 KOH
CON room temperature

PRO CP 851889-76-4, CQ 851889-77-5

NTE reaction monitored by TLC

RX(31) RCT CQ 851889-77-5
PRO CP 851889-76-4
CAT 24057-28-1 Pyridinium tosylate
SOL 75-09-2 CH₂Cl₂
NTE no reaction details

RX(32) RCT CP 851889-76-4

STAGE(1)

SOL 71-43-2 Benzene
CON room temperature

STAGE(2)

CAT 15529-49-4 RuCl₂(PPh₃)₃
CON 2 hours, room temperature

STAGE(3)

CAT 15529-49-4 RuCl₂(PPh₃)₃
CON 6 hours, room temperature

STAGE(4)

RGT CV 513-35-9 Me₂C:CHMe
SOL 75-65-0 t-BuOH
CON room temperature

STAGE(5)

RGT CW 7558-80-7 NaH₂PO₄, CX 7758-19-2 NaOClO
SOL 7732-18-5 Water
CON 1 hour, room temperature

STAGE(6)

RGT CW 7558-80-7 NaH₂PO₄, CX 7758-19-2 NaOClO
SOL 7732-18-5 Water
CON 1 hour, room temperature

STAGE(7)

SOL 60-29-7 Et₂O
CON room temperature

STAGE(8)

RGT C 7647-01-0 HCl
SOL 7732-18-5 Water
CON room temperature

STAGE(9)

SOL 67-56-1 MeOH, 71-43-2 Benzene
CON room temperature

STAGE(10)

RCT CT 18107-18-1
SOL 110-54-3 Hexane
CON 15 minutes, room temperature

PRO CU 851889-79-7

NTE last stage acidification

RX(33) RCT CU 851889-79-7

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STAGE(1)
  RGT  R 7087-68-5 EtN(Pr-i)2
  SOL  75-09-2 CH2Cl2
  CON  room temperature -> 0 deg C

STAGE(2)
  CAT  1122-58-3 4-DMAP
  CON  0 deg C

STAGE(3)
  RCT  N 107-30-2
  CON  SUBSTAGE(1) 0 deg C
      SUBSTAGE(2) 8 hours, 0 deg C -> room temperature

STAGE(4)
  RGT  D 144-55-8 NaHCO3
  SOL  7732-18-5 Water

PRO   DB 851889-80-0

RX(34)  RCT  DB 851889-80-0

  STAGE(1)
    SOL  110-54-3 Hexane
    CON  room temperature

  STAGE(2)
    CAT  91-22-5 Quinoline
    CON  room temperature

  STAGE(3)
    CAT  7440-05-3 Pd
    CON  room temperature

  STAGE(4)
    RGT  DC 1333-74-0 H2
    CON  8 hours, room temperature

  STAGE(5)
    SOL  107-14-2 ClCH2CN, 75-05-8 MeCN
    CON  room temperature

  STAGE(6)
    RGT  DD 516-12-1 Iodosuccinimide
    CON  3 hours, room temperature

  STAGE(7)
    RGT  DE 7772-98-7 Na2S2O3
    SOL  7732-18-5 Water
    CON  room temperature

PRO   M 851889-82-2
NTE   stereoselective; third stage Lindlar catalyst; sixth stage in
      dark; last stage quench

RX(3)  RCT  M 851889-82-2

  STAGE(1)
    SOL  109-99-9 THF
    CON  room temperature

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STAGE(2)
 RGT P 64-19-7 AcOH, Q 429-41-4 Bu4N.F
 SOL 109-99-9 THF
 CON 36 hours, room temperature

STAGE(3)
 SOL 7732-18-5 Water
 CON room temperature, pH 7

STAGE(4)
 RGT R 7087-68-5 EtN(Pr-i)2
 SOL 56-23-5 CCl4
 CON room temperature -> 0 deg C

STAGE(5)
 CAT 1122-58-3 4-DMAP
 CON 0 deg C

STAGE(6)
 RCT N 107-30-2
 CON SUBSTAGE(1) 0 deg C
 SUBSTAGE(2) 8 hours, 0 deg C -> room temperature

STAGE(7)
 RGT D 144-55-8 NaHCO3
 SOL 7732-18-5 Water

PRO O 851889-66-2
 NTE third stage quench

RX(35) RCT V ~~216669-69-1~~

STAGE(1)
 SOL 60-29-7 Et2O
 CON room temperature -> -78 deg C

STAGE(2)
 RGT DK 594-19-4 t-BuLi
 SOL 109-66-0 Pentane
 CON 30 minutes, -78 deg C

STAGE(3)
 RGT BO 7646-85-7 ZnCl2
 SOL 109-99-9 THF
 CON SUBSTAGE(1) 5 minutes, -78 deg C
 SUBSTAGE(2) 30 minutes, -78 deg C -> 0 deg C

STAGE(4)
 RCT O 851889-66-2
 CAT 14221-01-3 Pd(PPh3)4
 SOL 109-99-9 THF
 CON SUBSTAGE(1) 1 hour, 0 deg C
 SUBSTAGE(2) 0 deg C -> room temperature
 SUBSTAGE(3) 6 hours, room temperature

STAGE(5)
 SOL 7732-18-5 Water
 CON room temperature

PRO DJ 851889-85-5
 NTE last stage quench

RX(36) RCT DJ 851889-85-5

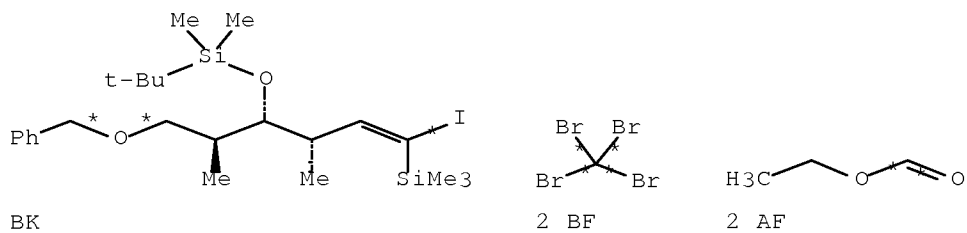
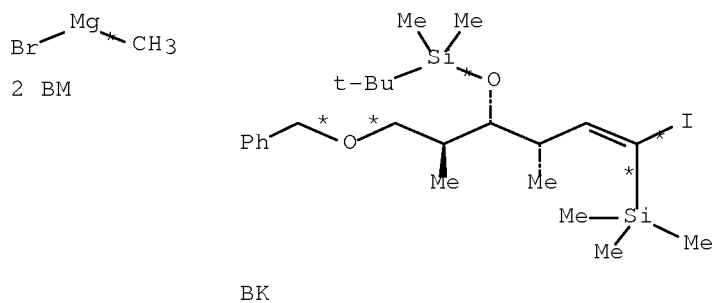
STAGE(1)
 SOL 67-56-1 MeOH
 CON room temperature -> 0 deg C

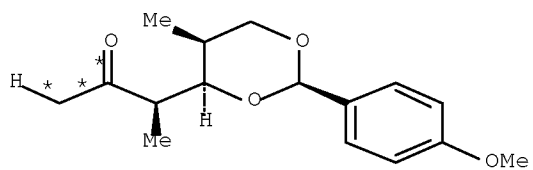
STAGE(2)
 CAT 104-15-4 TsOH
 CON 1 hour, 0 deg C

STAGE(3)
 RGT AR 121-44-8 Et3N
 CON 0 deg C

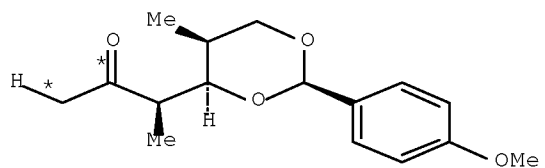
PRO G 851889-86-6
 NTE last stage quench

RX(530) OF 576 COMPOSED OF RX(15), RX(16), RX(17), RX(18), RX(6), RX(28),
 RX(29), RX(30), RX(32), RX(33), RX(34), RX(3), RX(35), RX(36), RX(2)
 RX(530) 2 BM + 2 BK + 2 BF + 2 AF + 2 AA + 2 CM + CT +
 2 N + V + H ==> I

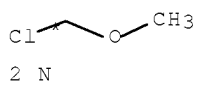
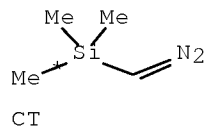
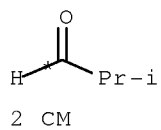




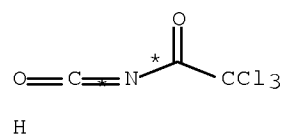
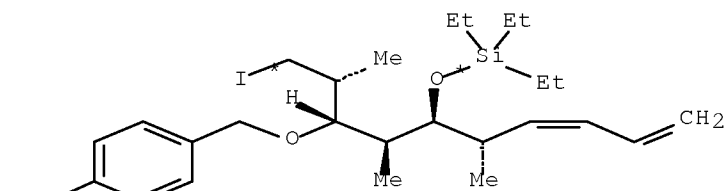
AA



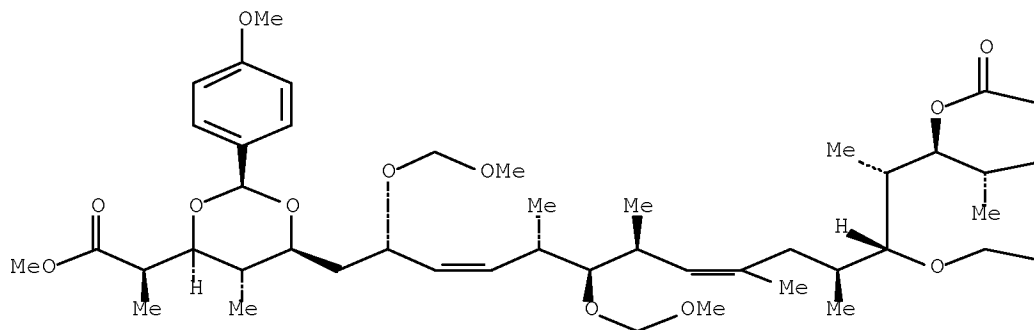
AA



V



15
STEPS
→



* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

RX(15)

STAGE(1)

RGT BO 7646-85-7 ZnCl₂

SOL 109-99-9 THF

CON room temperature

STAGE(2)

RCT BM 75-16-1

SOL 60-29-7 Et₂O

CON 15 minutes, room temperature

STAGE(3)

RCT BK 444109-29-9

CAT 14221-01-3 Pd(PPh₃)₄

SOL 109-99-9 THF

CON 2 hours, room temperature

STAGE(4)

RGT AI 12125-02-9 NH₄Cl

SOL 7732-18-5 Water

CON room temperature

PRO BN 444109-30-2

NTE key step, stereoselective; last stage quench

RX(16)

STAGE(1)

RGT BS 1625-91-8 (p-t-BuC₆H₄)₂

SOL 109-99-9 THF

CON room temperature

STAGE(2)

RGT BT 7439-93-2 Li

CON SUBSTAGE(1) room temperature

SUBSTAGE(2) room temperature -> 25 deg C

SUBSTAGE(3) 5 hours, 15 - 25 deg C

SUBSTAGE(4) 15 deg C -> room temperature

STAGE(3)
RCT BN 444109-30-2
SOL 109-99-9 THF
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) 2.5 hours, -78 deg C

STAGE(4)
RGT AI 12125-02-9 NH4Cl
SOL 7732-18-5 Water
CON -78 deg C -> room temperature

PRO BR 444109-31-3
NTE first stage sonication; third stage inverse addn.; last stage
quench

RX(17)

STAGE(1)
RGT AQ 79-37-8 (COCl)₂
SOL 75-09-2 CH₂Cl₂
CON room temperature -> -78 deg C

STAGE(2)
RGT AP 67-68-5 DMSO
CON 45 minutes, -78 deg C

STAGE(3)
RCT BR 444109-31-3
SOL 75-09-2 CH₂Cl₂
CON 1 hour, -78 deg C

STAGE(4)
RGT AR 121-44-8 Et₃N
CON SUBSTAGE(1) 15 minutes, -78 deg C
SUBSTAGE(2) 20 minutes, -78 deg C -> room temperature

PRO BU 444109-43-7
NTE last stage quench; Swern oxidn.

RX(18) RCT BF 558-13-4

STAGE(1)
RGT W 603-35-0 PPh₃
SOL 75-09-2 CH₂Cl₂
CON 10 minutes, 0 deg C

STAGE(2)
RCT BU 444109-43-7
RGT BH 108-48-5 2,6-Lutidine
SOL 75-09-2 CH₂Cl₂
CON 4 hours, 0 deg C

STAGE(3)
RGT AI 12125-02-9 NH₄Cl
SOL 7732-18-5 Water
CON 0 deg C

PRO AE 444109-32-4
NTE last stage quench; Corey-Fuchs olefination

RX(6) RCT AE 444109-32-4

STAGE(1)

SOL 109-99-9 THF
CON room temperature -> -78 deg C

STAGE(2)

RGT AH 109-72-8 BuLi
SOL 110-54-3 Hexane
CON SUBSTAGE(1) 30 minutes, -78 deg C
SUBSTAGE(2) -78 deg C -> -20 deg C
SUBSTAGE(3) 1 hour, -20 deg C
SUBSTAGE(4) -20 deg C -> -78 deg C

STAGE(3)

RCT AF 109-94-4
CON SUBSTAGE(1) 2 hours, -78 deg C
SUBSTAGE(2) -78 deg C -> 30 deg C
SUBSTAGE(3) 8 hours, 30 deg C

STAGE(4)

RGT AI 12125-02-9 NH4Cl
SOL 7732-18-5 Water
CON 30 deg C -> room temperature

PRO AG 444109-23-3
NTE last stage quench

RX(28) RCT AA 652986-45-3

STAGE(1)

SOL 75-09-2 CH2Cl2
CON room temperature -> -78 deg C

STAGE(2)

RGT R 7087-68-5 EtN(Pr-i)2
CON 5 minutes, -78 deg C

STAGE(3)

RGT CK 60669-69-4 F3CSO3BBu2
CON 45 minutes, -78 deg C

STAGE(4)

RCT AG 444109-23-3
SOL 75-09-2 CH2Cl2
CON 1 hour, -78 deg C

STAGE(5)

SOL 7732-18-5 Water, 67-56-1 MeOH
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> 0 deg C

STAGE(6)

RGT CL 7722-84-1 H2O2
SOL 7732-18-5 Water, 67-56-1 MeOH
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature

STAGE(7)

RGT D 144-55-8 NaHCO₃
SOL 7732-18-5 Water
CON room temperature

PRO CJ 851889-73-1
NTE key step, stereoselective (d.r. 30:1); fifth stage phosphate
buffer; aldol reaction

RX(29) RCT CJ 851889-73-1

STAGE(1)
SOL 109-99-9 THF
CON room temperature

STAGE(2)
RCT CM 78-84-2
CON room temperature -> -10 deg C

STAGE(3)
RGT CO 32248-43-4 SmI₂
SOL 109-99-9 THF
CON 4 hours, -10 deg C

STAGE(4)
RGT D 144-55-8 NaHCO₃
SOL 7732-18-5 Water
CON -10 deg C -> room temperature

PRO CN 851889-75-3
NTE last stage quench

RX(30) RCT CN 851889-75-3

STAGE(1)
SOL 67-56-1 MeOH
CON room temperature

STAGE(2)
RGT CR 1310-58-3 KOH
CON room temperature

PRO CP 851889-76-4, CQ 851889-77-5
NTE reaction monitored by TLC

RX(32) RCT CP 851889-76-4

STAGE(1)
SOL 71-43-2 Benzene
CON room temperature

STAGE(2)
CAT 15529-49-4 RuCl₂(PPh₃)₃
CON 2 hours, room temperature

STAGE(3)
CAT 15529-49-4 RuCl₂(PPh₃)₃
CON 6 hours, room temperature

STAGE(4)
RGT CV 513-35-9 Me₂C:CHMe

SOL 75-65-0 t-BuOH
CON room temperature

STAGE(5)

RGT CW 7558-80-7 NaH₂PO₄, CX 7758-19-2 NaOClO
SOL 7732-18-5 Water
CON 1 hour, room temperature

STAGE(6)

RGT CW 7558-80-7 NaH₂PO₄, CX 7758-19-2 NaOClO
SOL 7732-18-5 Water
CON 1 hour, room temperature

STAGE(7)

SOL 60-29-7 Et₂O
CON room temperature

STAGE(8)

RGT C 7647-01-0 HCl
SOL 7732-18-5 Water
CON room temperature

STAGE(9)

SOL 67-56-1 MeOH, 71-43-2 Benzene
CON room temperature

STAGE(10)

RCT CT 18107-18-1
SOL 110-54-3 Hexane
CON 15 minutes, room temperature

PRO CU 851889-79-7
NTE last stage acidification

RX(33) RCT CU 851889-79-7

STAGE(1)

RGT R 7087-68-5 EtN(Pr-i)₂
SOL 75-09-2 CH₂Cl₂
CON room temperature -> 0 deg C

STAGE(2)

CAT 1122-58-3 4-DMAP
CON 0 deg C

STAGE(3)

RCT N 107-30-2
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 8 hours, 0 deg C -> room temperature

STAGE(4)

RGT D 144-55-8 NaHCO₃
SOL 7732-18-5 Water

PRO DB 851889-80-0

RX(34) RCT DB 851889-80-0

STAGE(1)

SOL 110-54-3 Hexane

CON room temperature

STAGE(2)

CAT 91-22-5 Quinoline

CON room temperature

STAGE(3)

CAT 7440-05-3 Pd

CON room temperature

STAGE(4)

RGT DC 1333-74-0 H2

CON 8 hours, room temperature

STAGE(5)

SOL 107-14-2 ClCH2CN, 75-05-8 MeCN

CON room temperature

STAGE(6)

RGT DD 516-12-1 Iodosuccinimide

CON 3 hours, room temperature

STAGE(7)

RGT DE 7772-98-7 Na2S2O3

SOL 7732-18-5 Water

CON room temperature

PRO M 851889-82-2

NTE stereoselective; third stage Lindlar catalyst; sixth stage in dark; last stage quench

RX(3)

RCT M 851889-82-2

STAGE(1)

SOL 109-99-9 THF

CON room temperature

STAGE(2)

RGT P 64-19-7 AcOH, Q 429-41-4 Bu4N.F

SOL 109-99-9 THF

CON 36 hours, room temperature

STAGE(3)

SOL 7732-18-5 Water

CON room temperature, pH 7

STAGE(4)

RGT R 7087-68-5 EtN(Pr-i)2

SOL 56-23-5 CCl4

CON room temperature -> 0 deg C

STAGE(5)

CAT 1122-58-3 4-DMAP

CON 0 deg C

STAGE(6)

RCT N 107-30-2

CON SUBSTAGE(1) 0 deg C

SUBSTAGE(2) 8 hours, 0 deg C -> room temperature

```

    STAGE(7)
      RGT  D 144-55-8 NaHCO3
      SOL  7732-18-5 Water

PRO  O 851889-66-2
NTE  third stage quench

RX(35)  RCT  V 216669-69-1

    STAGE(1)
      SOL  60-29-7 Et2O
      CON  room temperature -> -78 deg C

    STAGE(2)
      RGT  DK 594-19-4 t-BuLi
      SOL  109-66-0 Pentane
      CON  30 minutes, -78 deg C

    STAGE(3)
      RGT  BO 7646-85-7 ZnCl2
      SOL  109-99-9 THF
      CON  SUBSTAGE(1) 5 minutes, -78 deg C
          SUBSTAGE(2) 30 minutes, -78 deg C -> 0 deg C

    STAGE(4)
      RCT  O 851889-66-2
      CAT  14221-01-3 Pd(PPh3)4
      SOL  109-99-9 THF
      CON  SUBSTAGE(1) 1 hour, 0 deg C
          SUBSTAGE(2) 0 deg C -> room temperature
          SUBSTAGE(3) 6 hours, room temperature

    STAGE(5)
      SOL  7732-18-5 Water
      CON  room temperature

PRO  DJ 851889-85-5
NTE  last stage quench

RX(36)  RCT  DJ 851889-85-5

    STAGE(1)
      SOL  67-56-1 MeOH
      CON  room temperature -> 0 deg C

    STAGE(2)
      CAT  104-15-4 TsOH
      CON  1 hour, 0 deg C

    STAGE(3)
      RGT  AR 121-44-8 Et3N
      CON  0 deg C

PRO  G 851889-86-6
NTE  last stage quench

RX(2)  RCT  G 851889-86-6

    STAGE(1)
      SOL  75-09-2 CH2Cl2

```

CON room temperature

STAGE(2)

RCT H 3019-71-4

CON 10 minutes, room temperature

STAGE(3)

SOL 67-56-1 MeOH

CON room temperature

STAGE(4)

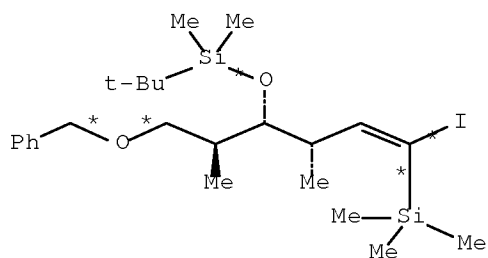
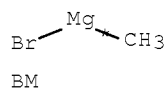
RGT J 584-08-7 K2CO3

CON 75 minutes, room temperature

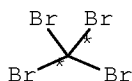
PRO I 851889-65-1

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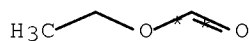
RX(567) BM + BK + BF + AF + AA + CM + CT + 2 N +
V + H ==> A



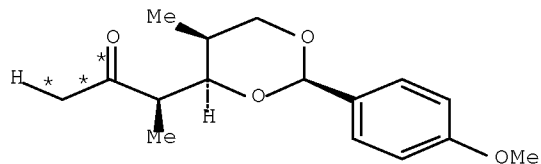
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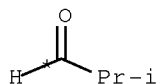
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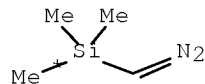
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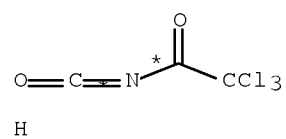
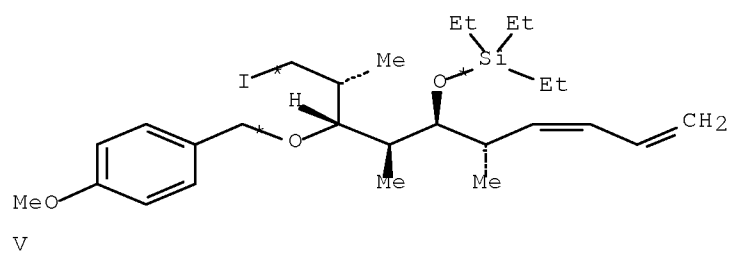
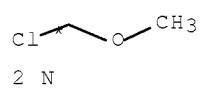
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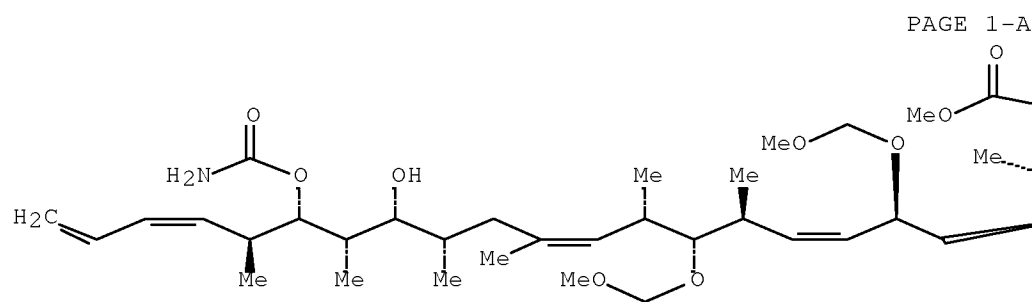
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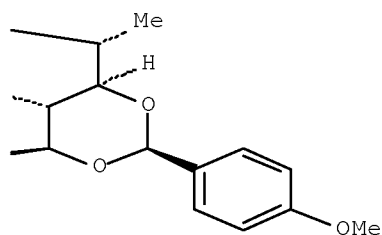


CT



16
 STEPS





A
YIELD 90%

RX(15)

STAGE(1)

RGT BO 7646-85-7 ZnCl₂
SOL 109-99-9 THF
CON room temperature

STAGE(2)

RCT BM 75-16-1
SOL 60-29-7 Et₂O
CON 15 minutes, room temperature

STAGE(3)

RCT BK 444109-29-9
CAT 14221-01-3 Pd(PPh₃)₄
SOL 109-99-9 THF
CON 2 hours, room temperature

STAGE(4)

RGT AI 12125-02-9 NH₄Cl
SOL 7732-18-5 Water
CON room temperature

PRO BN 444109-30-2

NTE key step, stereoselective; last stage quench

RX(16)

STAGE(1)

RGT BS 1625-91-8 (p-t-BuC₆H₄)₂
SOL 109-99-9 THF
CON room temperature

STAGE(2)

RGT BT 7439-93-2 Li
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) room temperature -> 25 deg C
SUBSTAGE(3) 5 hours, 15 - 25 deg C
SUBSTAGE(4) 15 deg C -> room temperature

STAGE(3)

RCT BN 444109-30-2

SOL 109-99-9 THF
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) 2.5 hours, -78 deg C

STAGE(4)
RGT AI 12125-02-9 NH4Cl
SOL 7732-18-5 Water
CON -78 deg C -> room temperature

PRO BR 444109-31-3
NTE first stage sonication; third stage inverse addn.; last stage
quench

RX(17)

STAGE(1)
RGT AQ 79-37-8 (COCl)₂
SOL 75-09-2 CH₂Cl₂
CON room temperature -> -78 deg C

STAGE(2)
RGT AP 67-68-5 DMSO
CON 45 minutes, -78 deg C

STAGE(3)
RCT BR 444109-31-3
SOL 75-09-2 CH₂Cl₂
CON 1 hour, -78 deg C

STAGE(4)
RGT AR 121-44-8 Et₃N
CON SUBSTAGE(1) 15 minutes, -78 deg C
SUBSTAGE(2) 20 minutes, -78 deg C -> room temperature

PRO BU 444109-43-7
NTE last stage quench; Swern oxidn.

RX(18) RCT BF 558-13-4

STAGE(1)
RGT W 603-35-0 PPh₃
SOL 75-09-2 CH₂Cl₂
CON 10 minutes, 0 deg C

STAGE(2)
RCT BU 444109-43-7
RGT BH 108-48-5 2,6-Lutidine
SOL 75-09-2 CH₂Cl₂
CON 4 hours, 0 deg C

STAGE(3)
RGT AI 12125-02-9 NH₄Cl
SOL 7732-18-5 Water
CON 0 deg C

PRO AE 444109-32-4
NTE last stage quench; Corey-Fuchs olefination

RX(6) RCT AE 444109-32-4

```

STAGE(1)
  SOL  109-99-9 THF
  CON  room temperature -> -78 deg C

STAGE(2)
  RGT  AH 109-72-8 BuLi
  SOL  110-54-3 Hexane
  CON  SUBSTAGE(1) 30 minutes, -78 deg C
      SUBSTAGE(2) -78 deg C -> -20 deg C
      SUBSTAGE(3) 1 hour, -20 deg C
      SUBSTAGE(4) -20 deg C -> -78 deg C

STAGE(3)
  RCT  AF 109-94-4
  CON  SUBSTAGE(1) 2 hours, -78 deg C
      SUBSTAGE(2) -78 deg C -> 30 deg C
      SUBSTAGE(3) 8 hours, 30 deg C

STAGE(4)
  RGT  AI 12125-02-9 NH4Cl
  SOL  7732-18-5 Water
  CON  30 deg C -> room temperature

PRO  AG 444109-23-3
NTE  last stage quench

RX(28)  RCT  AA 652986-45-3

STAGE(1)
  SOL  75-09-2 CH2Cl2
  CON  room temperature -> -78 deg C

STAGE(2)
  RGT  R 7087-68-5 EtN(Pr-i)2
  CON  5 minutes, -78 deg C

STAGE(3)
  RGT  CK 60669-69-4 F3CSO3BBu2
  CON  45 minutes, -78 deg C

STAGE(4)
  RCT  AG 444109-23-3
  SOL  75-09-2 CH2Cl2
  CON  1 hour, -78 deg C

STAGE(5)
  SOL  7732-18-5 Water, 67-56-1 MeOH
  CON  SUBSTAGE(1) -78 deg C
      SUBSTAGE(2) -78 deg C -> 0 deg C

STAGE(6)
  RGT  CL 7722-84-1 H2O2
  SOL  7732-18-5 Water, 67-56-1 MeOH
  CON  SUBSTAGE(1) 1 hour, 0 deg C
      SUBSTAGE(2) 0 deg C -> room temperature

STAGE(7)
  RGT  D 144-55-8 NaHCO3
  SOL  7732-18-5 Water
  CON  room temperature

```

PRO CJ 851889-73-1
NTE key step, stereoselective (d.r. 30:1); fifth stage phosphate
buffer; aldol reaction

RX(29) RCT CJ 851889-73-1

STAGE(1)

SOL 109-99-9 THF
CON room temperature

STAGE(2)

RCT CM 78-84-2
CON room temperature -> -10 deg C

STAGE(3)

RGT CO 32248-43-4 SmI2
SOL 109-99-9 THF
CON 4 hours, -10 deg C

STAGE(4)

RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water
CON -10 deg C -> room temperature

PRO CN 851889-75-3
NTE last stage quench

RX(30) RCT CN 851889-75-3

STAGE(1)

SOL 67-56-1 MeOH
CON room temperature

STAGE(2)

RGT CR 1310-58-3 KOH
CON room temperature

PRO CP 851889-76-4, CQ 851889-77-5
NTE reaction monitored by TLC

RX(32) RCT CP 851889-76-4

STAGE(1)

SOL 71-43-2 Benzene
CON room temperature

STAGE(2)

CAT 15529-49-4 RuCl2(PPh3)3
CON 2 hours, room temperature

STAGE(3)

CAT 15529-49-4 RuCl2(PPh3)3
CON 6 hours, room temperature

STAGE(4)

RGT CV 513-35-9 Me2C:CHMe
SOL 75-65-0 t-BuOH
CON room temperature

STAGE(5)
RGT CW 7558-80-7 NaH2PO4, CX 7758-19-2 NaOClO
SOL 7732-18-5 Water
CON 1 hour, room temperature

STAGE(6)
RGT CW 7558-80-7 NaH2PO4, CX 7758-19-2 NaOClO
SOL 7732-18-5 Water
CON 1 hour, room temperature

STAGE(7)
SOL 60-29-7 Et2O
CON room temperature

STAGE(8)
RGT C 7647-01-0 HCl
SOL 7732-18-5 Water
CON room temperature

STAGE(9)
SOL 67-56-1 MeOH, 71-43-2 Benzene
CON room temperature

STAGE(10)
RCT CT 18107-18-1
SOL 110-54-3 Hexane
CON 15 minutes, room temperature

PRO CU 851889-79-7
NTE last stage acidification

RX(33) RCT CU 851889-79-7

STAGE(1)
RGT R 7087-68-5 EtN(Pr-i)2
SOL 75-09-2 CH2Cl2
CON room temperature -> 0 deg C

STAGE(2)
CAT 1122-58-3 4-DMAP
CON 0 deg C

STAGE(3)
RCT N 107-30-2
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 8 hours, 0 deg C -> room temperature

STAGE(4)
RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water

PRO DB 851889-80-0

RX(34) RCT DB 851889-80-0

STAGE(1)
SOL 110-54-3 Hexane
CON room temperature

STAGE(2)

CAT 91-22-5 Quinoline
CON room temperature

STAGE(3)

CAT 7440-05-3 Pd
CON room temperature

STAGE(4)

RGT DC 1333-74-0 H2
CON 8 hours, room temperature

STAGE(5)

SOL 107-14-2 ClCH2CN, 75-05-8 MeCN
CON room temperature

STAGE(6)

RGT DD 516-12-1 Iodosuccinimide
CON 3 hours, room temperature

STAGE(7)

RGT DE 7772-98-7 Na2S2O3
SOL 7732-18-5 Water
CON room temperature

PRO M 851889-82-2

NTE stereoselective; third stage Lindlar catalyst; sixth stage in
dark; last stage quench

RX(3)

RCT M 851889-82-2

STAGE(1)

SOL 109-99-9 THF
CON room temperature

STAGE(2)

RGT P 64-19-7 AcOH, Q 429-41-4 Bu4N.F
SOL 109-99-9 THF
CON 36 hours, room temperature

STAGE(3)

SOL 7732-18-5 Water
CON room temperature, pH 7

STAGE(4)

RGT R 7087-68-5 EtN(Pr-i)2
SOL 56-23-5 CCl4
CON room temperature -> 0 deg C

STAGE(5)

CAT 1122-58-3 4-DMAP
CON 0 deg C

STAGE(6)

RCT N 107-30-2
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 8 hours, 0 deg C -> room temperature

STAGE(7)

RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water

PRO O 851889-66-2
NTE third stage quench

RX(35) RCT V ~~216669-69-1~~

STAGE(1)
SOL 60-29-7 Et2O
CON room temperature -> -78 deg C

STAGE(2)
RGT DK 594-19-4 t-BuLi
SOL 109-66-0 Pentane
CON 30 minutes, -78 deg C

STAGE(3)
RGT BO 7646-85-7 ZnCl2
SOL 109-99-9 THF
CON SUBSTAGE(1) 5 minutes, -78 deg C
SUBSTAGE(2) 30 minutes, -78 deg C -> 0 deg C

STAGE(4)
RCT O 851889-66-2
CAT 14221-01-3 Pd(PPh3)4
SOL 109-99-9 THF
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature
SUBSTAGE(3) 6 hours, room temperature

STAGE(5)
SOL 7732-18-5 Water
CON room temperature

PRO DJ 851889-85-5
NTE last stage quench

RX(36) RCT DJ 851889-85-5

STAGE(1)
SOL 67-56-1 MeOH
CON room temperature -> 0 deg C

STAGE(2)
CAT 104-15-4 TsOH
CON 1 hour, 0 deg C

STAGE(3)
RGT AR 121-44-8 Et3N
CON 0 deg C

PRO G 851889-86-6
NTE last stage quench

RX(2) RCT G 851889-86-6

STAGE(1)
SOL 75-09-2 CH2Cl2
CON room temperature

STAGE(2)

RCT H 3019-71-4
 CON 10 minutes, room temperature

STAGE(3)
 SOL 67-56-1 MeOH
 CON room temperature

STAGE(4)
 RGT J 584-08-7 K2CO3
 CON 75 minutes, room temperature

PRO I 851889-65-1

RX(37) RCT I 851889-65-1

STAGE(1)
 SOL 7732-18-5 Water, 75-09-2 CH2Cl2
 CON room temperature

STAGE(2)
 RGT D 144-55-8 NaHCO3
 CON room temperature

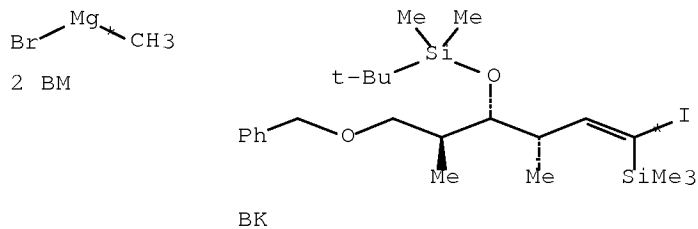
STAGE(3)
 RGT DM 84-58-2 DDQ
 SOL 75-09-2 CH2Cl2
 CON 1 hour, room temperature

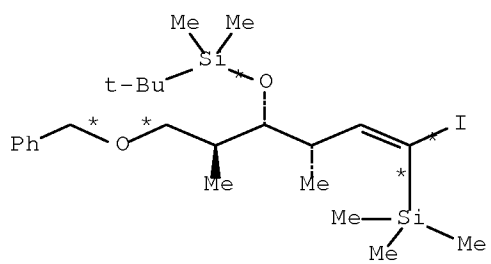
STAGE(4)
 RGT DM 84-58-2 DDQ
 SOL 75-09-2 CH2Cl2
 CON 1 hour, room temperature

PRO A 851889-87-7

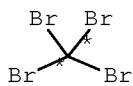
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RX(568) 2 BM + 2 BK + BF + 2 AF + 2 AA + CM + CT + 2
 N + V + H ==> I

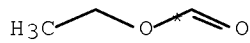




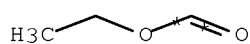
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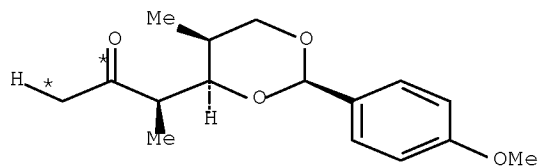
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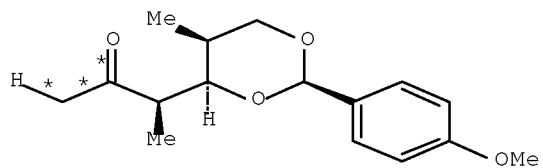
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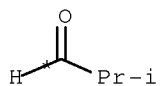
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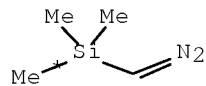
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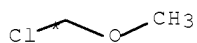
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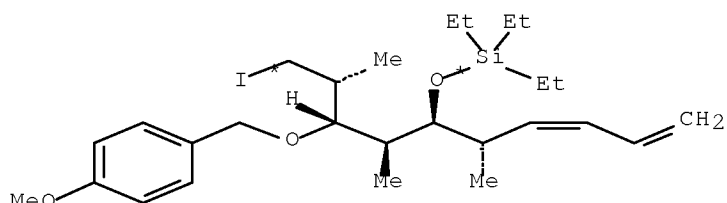
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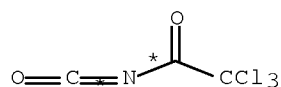
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2 N



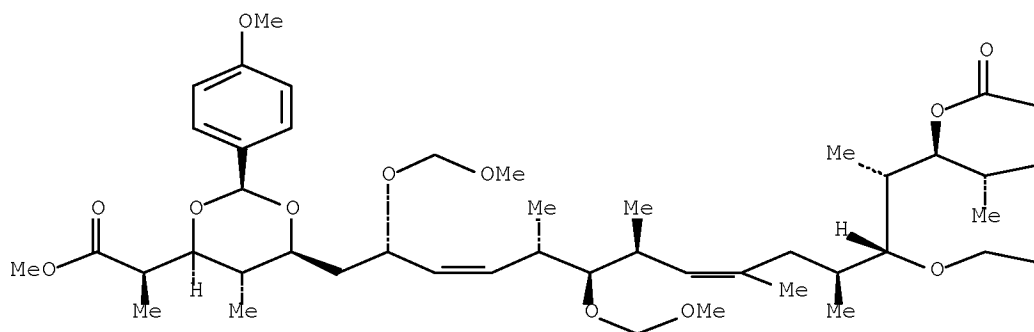
V



H

16
STEPS
→

PAGE 1-A



* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

RX(15)

STAGE(1)

RGT BO 7646-85-7 ZnCl₂
SOL 109-99-9 THF
CON room temperature

STAGE(2)

RCT BM 75-16-1
SOL 60-29-7 Et₂O
CON 15 minutes, room temperature

STAGE(3)

RCT BK 444109-29-9
CAT 14221-01-3 Pd(PPh₃)₄
SOL 109-99-9 THF
CON 2 hours, room temperature

STAGE(4)

RGT AI 12125-02-9 NH₄Cl
SOL 7732-18-5 Water
CON room temperature

PRO BN 444109-30-2

NTE key step, stereoselective; last stage quench

RX(16)

```
STAGE(1)
  RGT  BS 1625-91-8 (p-t-BuC6H4)2
  SOL  109-99-9 THF
  CON  room temperature

STAGE(2)
  RGT  BT 7439-93-2 Li
  CON  SUBSTAGE(1) room temperature
      SUBSTAGE(2) room temperature -> 25 deg C
      SUBSTAGE(3) 5 hours, 15 - 25 deg C
      SUBSTAGE(4) 15 deg C -> room temperature

STAGE(3)
  RCT  BN 444109-30-2
  SOL  109-99-9 THF
  CON  SUBSTAGE(1) room temperature -> -78 deg C
      SUBSTAGE(2) 2.5 hours, -78 deg C

STAGE(4)
  RGT  AI 12125-02-9 NH4Cl
  SOL  7732-18-5 Water
  CON  -78 deg C -> room temperature

PRO  BR 444109-31-3
NTE  first stage sonication; third stage inverse addn.; last stage
     quench
```

RX(17)

```
STAGE(1)
  RGT  AQ 79-37-8 (COCl)2
  SOL  75-09-2 CH2Cl2
  CON  room temperature -> -78 deg C

STAGE(2)
  RGT  AP 67-68-5 DMSO
  CON  45 minutes, -78 deg C

STAGE(3)
  RCT  BR 444109-31-3
  SOL  75-09-2 CH2Cl2
  CON  1 hour, -78 deg C

STAGE(4)
  RGT  AR 121-44-8 Et3N
  CON  SUBSTAGE(1) 15 minutes, -78 deg C
      SUBSTAGE(2) 20 minutes, -78 deg C -> room temperature

PRO  BU 444109-43-7
NTE  last stage quench; Swern oxidn.
```

RX(18)

```
RCT  BF 558-13-4

STAGE(1)
  RGT  W 603-35-0 PPh3
  SOL  75-09-2 CH2Cl2
  CON  10 minutes, 0 deg C
```

STAGE(2)
RCT BU 444109-43-7
RGT BH 108-48-5 2,6-Lutidine
SOL 75-09-2 CH2Cl2
CON 4 hours, 0 deg C

STAGE(3)
RGT AI 12125-02-9 NH4Cl
SOL 7732-18-5 Water
CON 0 deg C

PRO AE 444109-32-4
NTE last stage quench; Corey-Fuchs olefination

RX(6) RCT AE 444109-32-4

STAGE(1)
SOL 109-99-9 THF
CON room temperature -> -78 deg C

STAGE(2)
RGT AH 109-72-8 BuLi
SOL 110-54-3 Hexane
CON SUBSTAGE(1) 30 minutes, -78 deg C
SUBSTAGE(2) -78 deg C -> -20 deg C
SUBSTAGE(3) 1 hour, -20 deg C
SUBSTAGE(4) -20 deg C -> -78 deg C

STAGE(3)
RCT AF 109-94-4
CON SUBSTAGE(1) 2 hours, -78 deg C
SUBSTAGE(2) -78 deg C -> 30 deg C
SUBSTAGE(3) 8 hours, 30 deg C

STAGE(4)
RGT AI 12125-02-9 NH4Cl
SOL 7732-18-5 Water
CON 30 deg C -> room temperature

PRO AG 444109-23-3
NTE last stage quench

RX(28) RCT AA 652986-45-3

STAGE(1)
SOL 75-09-2 CH2Cl2
CON room temperature -> -78 deg C

STAGE(2)
RGT R 7087-68-5 EtN(Pr-i)2
CON 5 minutes, -78 deg C

STAGE(3)
RGT CK 60669-69-4 F3CSO3BBu2
CON 45 minutes, -78 deg C

STAGE(4)
RCT AG 444109-23-3
SOL 75-09-2 CH2Cl2
CON 1 hour, -78 deg C

STAGE(5)
 SOL 7732-18-5 Water, 67-56-1 MeOH
 CON SUBSTAGE(1) -78 deg C
 SUBSTAGE(2) -78 deg C -> 0 deg C

STAGE(6)
 RGT CL 7722-84-1 H2O2
 SOL 7732-18-5 Water, 67-56-1 MeOH
 CON SUBSTAGE(1) 1 hour, 0 deg C
 SUBSTAGE(2) 0 deg C -> room temperature

STAGE(7)
 RGT D 144-55-8 NaHCO3
 SOL 7732-18-5 Water
 CON room temperature

PRO CJ 851889-73-1
 NTE key step, stereoselective (d.r. 30:1); fifth stage phosphate
 buffer; aldol reaction

RX(29) RCT CJ 851889-73-1

 STAGE(1)
 SOL 109-99-9 THF
 CON room temperature

 STAGE(2)
 RCT CM 78-84-2
 CON room temperature -> -10 deg C

 STAGE(3)
 RGT CO 32248-43-4 SmI2
 SOL 109-99-9 THF
 CON 4 hours, -10 deg C

 STAGE(4)
 RGT D 144-55-8 NaHCO3
 SOL 7732-18-5 Water
 CON -10 deg C -> room temperature

PRO CN 851889-75-3
 NTE last stage quench

RX(30) RCT CN 851889-75-3

 STAGE(1)
 SOL 67-56-1 MeOH
 CON room temperature

 STAGE(2)
 RGT CR 1310-58-3 KOH
 CON room temperature

PRO CP 851889-76-4, CQ 851889-77-5
 NTE reaction monitored by TLC

RX(31) RCT CQ 851889-77-5
 PRO CP 851889-76-4
 CAT 24057-28-1 Pyridinium tosylate

SOL 75-09-2 CH₂Cl₂
NTE no reaction details

RX(32) RCT CP 851889-76-4

STAGE(1)

SOL 71-43-2 Benzene
CON room temperature

STAGE(2)

CAT 15529-49-4 RuCl₂(PPh₃)₃
CON 2 hours, room temperature

STAGE(3)

CAT 15529-49-4 RuCl₂(PPh₃)₃
CON 6 hours, room temperature

STAGE(4)

RGT CV 513-35-9 Me₂C:CHMe
SOL 75-65-0 t-BuOH
CON room temperature

STAGE(5)

RGT CW 7558-80-7 NaH₂PO₄, CX 7758-19-2 NaOClO
SOL 7732-18-5 Water
CON 1 hour, room temperature

STAGE(6)

RGT CW 7558-80-7 NaH₂PO₄, CX 7758-19-2 NaOClO
SOL 7732-18-5 Water
CON 1 hour, room temperature

STAGE(7)

SOL 60-29-7 Et₂O
CON room temperature

STAGE(8)

RGT C 7647-01-0 HCl
SOL 7732-18-5 Water
CON room temperature

STAGE(9)

SOL 67-56-1 MeOH, 71-43-2 Benzene
CON room temperature

STAGE(10)

RCT CT 18107-18-1
SOL 110-54-3 Hexane
CON 15 minutes, room temperature

PRO CU 851889-79-7
NTE last stage acidification

RX(33) RCT CU 851889-79-7

STAGE(1)

RGT R 7087-68-5 EtN(Pr-i)₂
SOL 75-09-2 CH₂Cl₂
CON room temperature -> 0 deg C

```

STAGE(2)
  CAT  1122-58-3 4-DMAP
  CON  0 deg C

STAGE(3)
  RCT  N 107-30-2
  CON  SUBSTAGE(1) 0 deg C
      SUBSTAGE(2) 8 hours, 0 deg C -> room temperature

STAGE(4)
  RGT  D 144-55-8 NaHCO3
  SOL  7732-18-5 Water

PRO   DB 851889-80-0

RX(34)  RCT  DB 851889-80-0

STAGE(1)
  SOL  110-54-3 Hexane
  CON  room temperature

STAGE(2)
  CAT  91-22-5 Quinoline
  CON  room temperature

STAGE(3)
  CAT  7440-05-3 Pd
  CON  room temperature

STAGE(4)
  RGT  DC 1333-74-0 H2
  CON  8 hours, room temperature

STAGE(5)
  SOL  107-14-2 ClCH2CN, 75-05-8 MeCN
  CON  room temperature

STAGE(6)
  RGT  DD 516-12-1 Iodosuccinimide
  CON  3 hours, room temperature

STAGE(7)
  RGT  DE 7772-98-7 Na2S2O3
  SOL  7732-18-5 Water
  CON  room temperature

PRO   M 851889-82-2
NTE   stereoselective; third stage Lindlar catalyst; sixth stage in
      dark; last stage quench

RX(3)  RCT  M 851889-82-2

STAGE(1)
  SOL  109-99-9 THF
  CON  room temperature

STAGE(2)
  RGT  P 64-19-7 AcOH, Q 429-41-4 Bu4N.F
  SOL  109-99-9 THF
  CON  36 hours, room temperature

```

STAGE(3)
SOL 7732-18-5 Water
CON room temperature, pH 7

STAGE(4)
RGT R 7087-68-5 EtN(Pr-i)2
SOL 56-23-5 CCl4
CON room temperature -> 0 deg C

STAGE(5)
CAT 1122-58-3 4-DMAP
CON 0 deg C

STAGE(6)
RCT N 107-30-2
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 8 hours, 0 deg C -> room temperature

STAGE(7)
RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water

PRO O 851889-66-2
NTE third stage quench

RX(35) RCT V 216669-69-1

STAGE(1)
SOL 60-29-7 Et2O
CON room temperature -> -78 deg C

STAGE(2)
RGT DK 594-19-4 t-BuLi
SOL 109-66-0 Pentane
CON 30 minutes, -78 deg C

STAGE(3)
RGT BO 7646-85-7 ZnCl2
SOL 109-99-9 THF
CON SUBSTAGE(1) 5 minutes, -78 deg C
SUBSTAGE(2) 30 minutes, -78 deg C -> 0 deg C

STAGE(4)
RCT O 851889-66-2
CAT 14221-01-3 Pd(PPh3)4
SOL 109-99-9 THF
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature
SUBSTAGE(3) 6 hours, room temperature

STAGE(5)
SOL 7732-18-5 Water
CON room temperature

PRO DJ 851889-85-5
NTE last stage quench

RX(36) RCT DJ 851889-85-5

STAGE(1)
SOL 67-56-1 MeOH
CON room temperature -> 0 deg C

STAGE(2)
CAT 104-15-4 TsOH
CON 1 hour, 0 deg C

STAGE(3)
RGT AR 121-44-8 Et3N
CON 0 deg C

PRO G 851889-86-6
NTE last stage quench

RX(2) RCT G 851889-86-6

STAGE(1)
SOL 75-09-2 CH2Cl2
CON room temperature

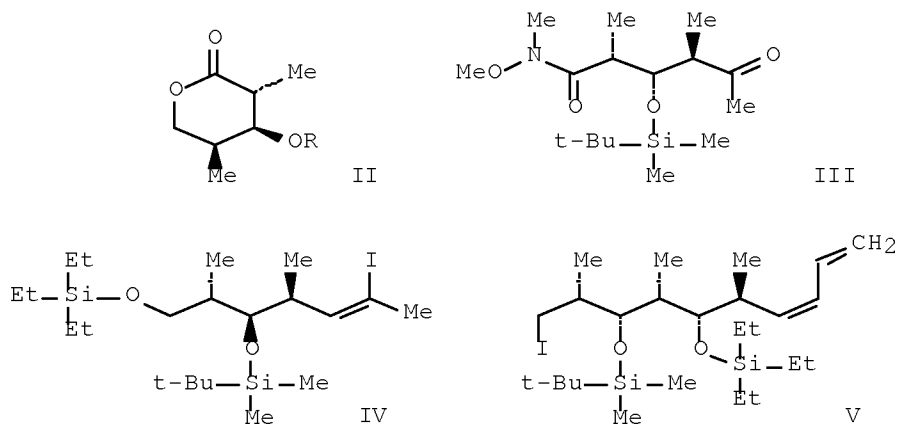
STAGE(2)
RCT H 3019-71-4
CON 10 minutes, room temperature

STAGE(3)
SOL 67-56-1 MeOH
CON room temperature

STAGE(4)
RGT J 584-08-7 K2CO3
CON 75 minutes, room temperature

PRO I 851889-65-1

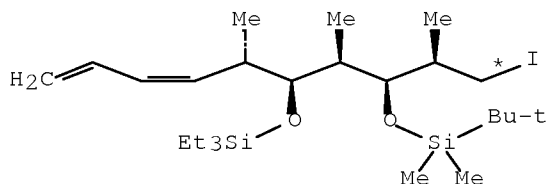
L3 ANSWER 7 OF 9 CASREACT COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 142:447055 CASREACT Full-text
TITLE: A Formal Synthesis of (+)-Discodermolide
AUTHOR(S): Loiseleur, Olivier; Koch, Guido; Cercus, Jacques;
Schuerch, Friedrich
CORPORATE SOURCE: Chemical and Analytical Development, Novartis Pharma
AG, Basel, CH-4002, Switz.
SOURCE: Organic Process Research & Development (2005), 9(3),
259-271
CODEN: OPRDFK; ISSN: 1083-6160
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



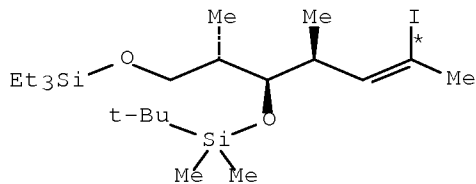
AB Herein, we report the formal synthesis of (+)-discodermolide (I), a promising anticancer agent of sponge origin, in 24 linear steps, with 35 steps in total. The route proceeds from lactone II (R = SiMe₂CMe₃, SiEt₃), a building block containing the common 1,2-anti-2,3-syn stereotriad found in each of the three subunits, Me ketone III (C1-C6), vinyl iodide IV (C9-C14), and iodide V (C15-C24) utilized for the construction of I. The key fragment union was achieved by a Suzuki cross-coupling between IV and V.

REFERENCE COUNT: 70 THERE ARE 70 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(17) OF 86 ...R + N ==> BE...

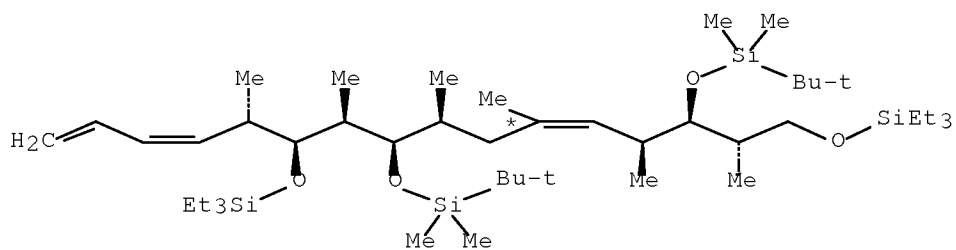


R



N





BE
YIELD 81%

RX(17) RCT R 649755-91-9

STAGE(1)

RGT BF 594-19-4 t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane
CON 5 minutes, -80 - -75 deg C

STAGE(2)

RGT BG 38050-71-4 9-BBN-OMe
SOL 109-99-9 THF
CON SUBSTAGE(1) 5 minutes, -80 - -75 deg C
SUBSTAGE(2) 90 minutes, -80 - -75 deg C -> 23 deg C

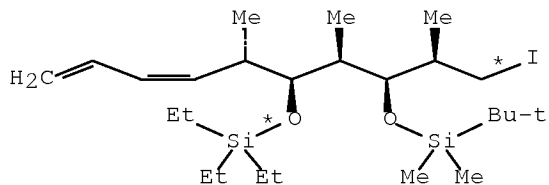
STAGE(3)

RCT N 851316-82-0
RGT BH 534-17-8 Cs2CO3
CAT 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON SUBSTAGE(1) 30 minutes, 23 deg C
SUBSTAGE(2) 30 minutes, 23 deg C

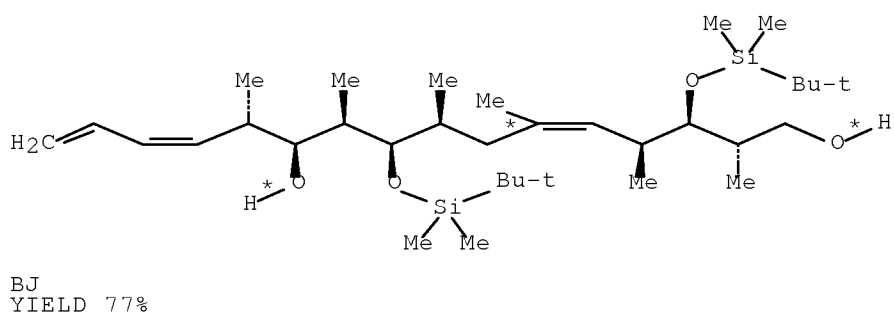
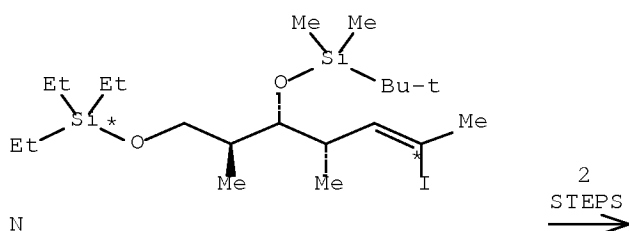
PRO BE 649755-93-1
NTE stereoselective

RX(33) OF 86 COMPOSED OF RX(17), RX(18)

RX(33) R + N ==> BJ



R



RX(17) RCT R 649755-91-9

STAGE(1)

RGT BF 594-19-4 t-BuLi
 SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane
 CON 5 minutes, -80 - -75 deg C

STAGE(2)

RGT BG 38050-71-4 9-BBN-OMe
 SOL 109-99-9 THF
 CON SUBSTAGE(1) 5 minutes, -80 - -75 deg C
 SUBSTAGE(2) 90 minutes, -80 - -75 deg C -> 23 deg C

STAGE(3)

RCT N 851316-82-0
 RGT BH 534-17-8 Cs2CO3
 CAT 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON SUBSTAGE(1) 30 minutes, 23 deg C
 SUBSTAGE(2) 30 minutes, 23 deg C

PRO BE 649755-93-1
 NTE stereoselective

RX(18) RCT BE 649755-93-1
 RGT BK 76-05-1 F3CCO2H

PRO BJ 261968--23--4
SOL 7732-18-5 Water, 109-99-9 THF
CON SUBSTAGE(1) 23 deg C
SUBSTAGE(2) 17 hours, 23 deg C
NTE chemoselective

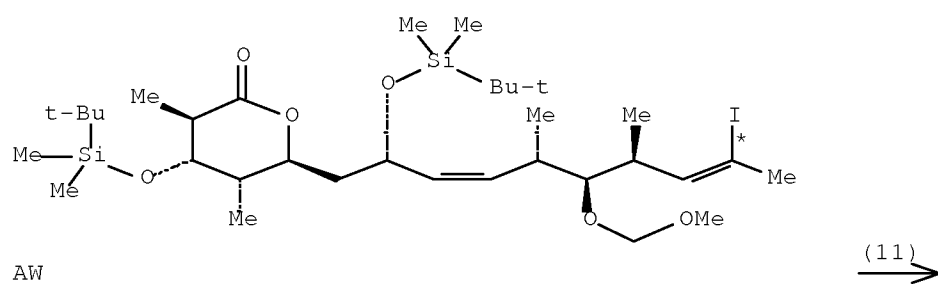
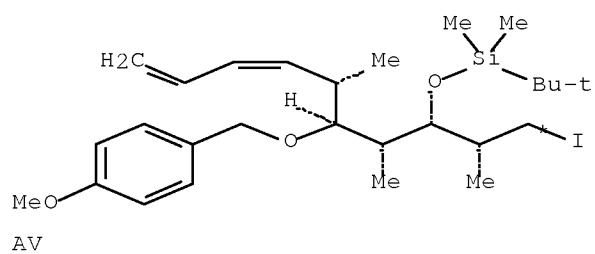
L3 ANSWER 8 OF 9 CASREACT COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 142:411149 CASREACT Full-text
TITLE: Synthesis of discodermolide and variants thereof
INVENTOR(S): Smith, Amos B., III; Freeze, Brian Scott; Xian, Ming
PATENT ASSIGNEE(S): The Trustees of the University of Pennsylvania, USA
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2005035489	A2	20050421	WO 2004-US33473	20041012
WO 2005035489	A3	20050804		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 20070276144	A1	20071129	US 2007-575136	20070509
PRIORITY APPLN. INFO.:			US 2003-510097P	20031009
			WO 2004-US33473	20041012
OTHER SOURCE(S):	MARPAT 142:411149			
GI				

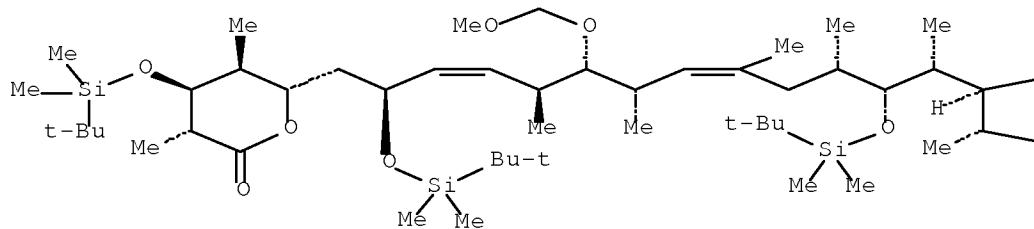
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Processes for synthesizing discodermolide and variants thereof such as I [R0 = alkyl, alkenyl, alkynyl, (CH2)ncycloalkyl, (CH2)naryl, (CH2)nheterocycle, wherein n = 0-4; R1, R2, R3, R6, R7, R8, R11, R12 = H, alkyl; R4, R9, R14, R15 = H, an acid labile hydroxyl protecting group; R10 = H, alkyl; R25 = H, an oxidation labile hydroxyl protecting group; Y = O, H2], are provided by reacting II with III [X1, X2 = halo, triflate, tosylate, mesylate]. Thus, intermediate I [R0 = CH:CH2; R1, R2, R3, R6, R7, R8, R11, R12 = Me; R4, R14, R15 = TBS; R9 = MOM; R25 = PMB; Y = O (IV)], was prepared via a multistep synthetic sequence starting from methyl-(2S)-3-hydroxy-2-methyl-propionate. The synthetic utility of IV was subsequently demonstrated by its use in the preparation of (+)-discodermolide.

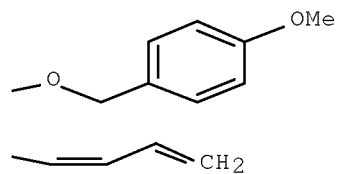
RX(11) OF 354 ...AV + AW ==> AX...



PAGE 1-A



PAGE 1-B



AX
YIELD 50%

RX(11) RCT AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) -78 deg C
SUBSTAGE(3) -78 deg C -> room temperature
SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

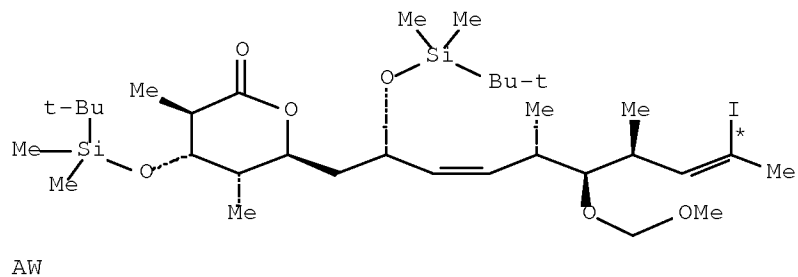
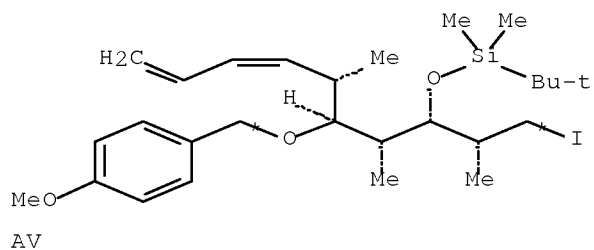
RCT AW 850211-74-4
RGT BA 534-17-8 Cs2CO3
CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

PRO AX 633293-75-1

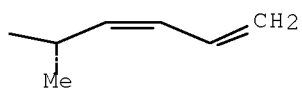
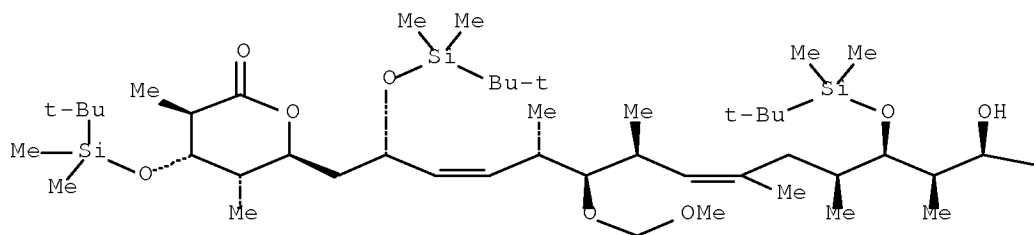
NTE BBN related byproducts were obtained in 10% yield, Suzuki
coupling

RX(44) OF 354 COMPOSED OF RX(11), RX(28)

RX(44) AV + AW ==> CO



2
STEPS
→



CO
YIELD 91%

RX(11) RCT AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
 SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0 Pentane
 CON SUBSTAGE(1) room temperature -> -78 deg C
 SUBSTAGE(2) -78 deg C
 SUBSTAGE(3) -78 deg C -> room temperature
 SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AW 850211-74-4
 RGT BA 534-17-8 Cs2CO3
 CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

PRO AX 633293-75-1

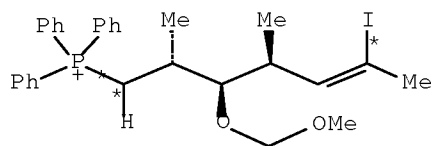
NTE BBN related byproducts were obtained in 10% yield, Suzuki coupling

RX(28) RCT AX 633293-75-1
 RGT CC 84-58-2 DDQ
 PRO CO 633293-76-2
 SOL 7732-18-5 Water, 75-09-2 CH2Cl2

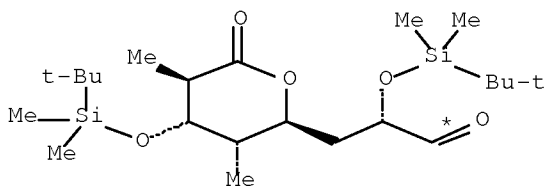
CON 0 - room temperature deg C

RX(61) OF 354 COMPOSED OF RX(27), RX(11)

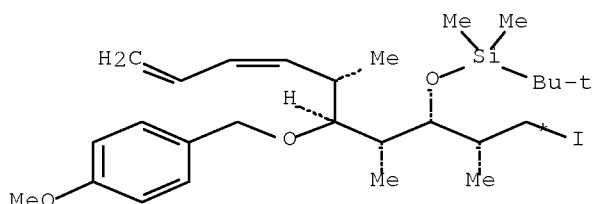
RX(61) CE + CN + AV ==> AX



CE

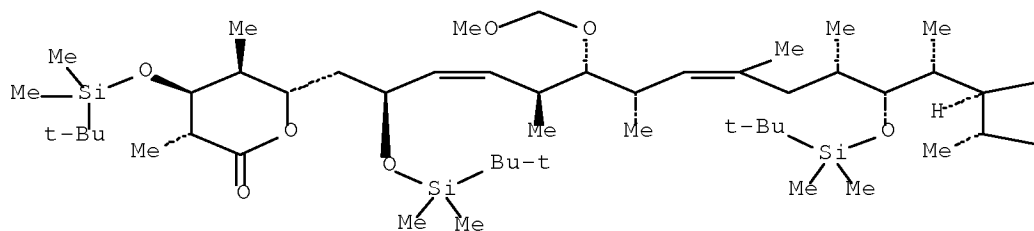


CN

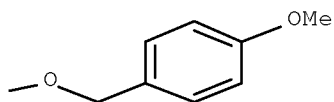


AV

2
STEPS
→



PAGE 1-A



AX
YIELD 50%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
 RGT CA 1070-89-9 (Me3Si)2N.Na
 PRO AW 850211-74-4
 CON -78 deg C -> -10 deg C
 NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
 SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0 Pentane
 CON SUBSTAGE(1) room temperature -> -78 deg C
 SUBSTAGE(2) -78 deg C
 SUBSTAGE(3) -78 deg C -> room temperature
 SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

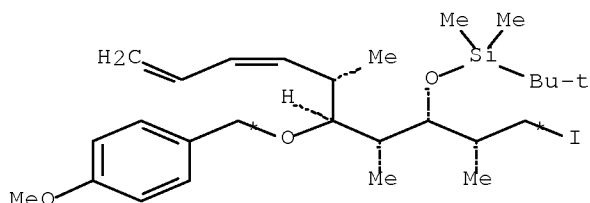
RCT AW 850211-74-4
 RGT BA 534-17-8 Cs2CO3
 CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

PRO AX 633293-75-1

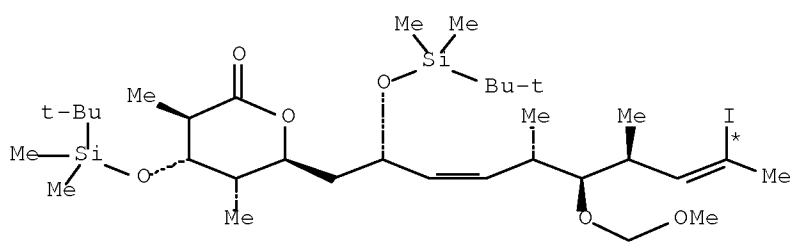
NTE BBN related byproducts were obtained in 10% yield, Suzuki coupling

RX(87) OF 354 COMPOSED OF RX(11), RX(28), RX(29)

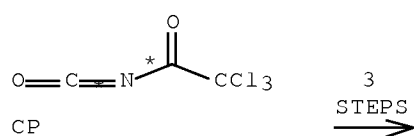
RX(87) AV + AW + CP ==> CQ



AV

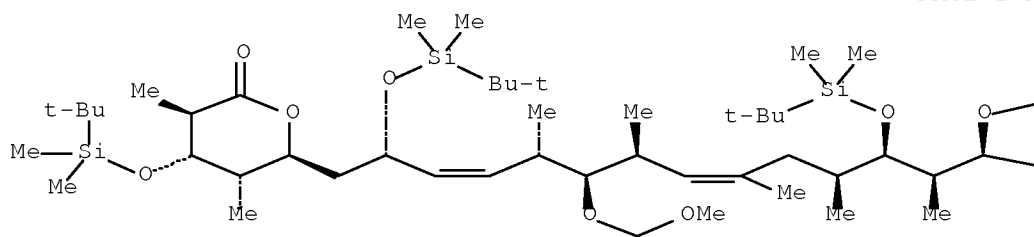


AW

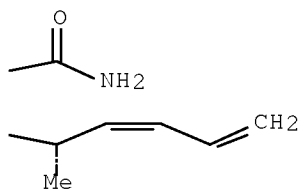


CP

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CQ
YIELD 92%

RX(11) RCT AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) -78 deg C
SUBSTAGE(3) -78 deg C -> room temperature
SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AW 850211-74-4
RGT BA 534-17-8 Cs2CO3
CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

PRO AX 633293-75-1

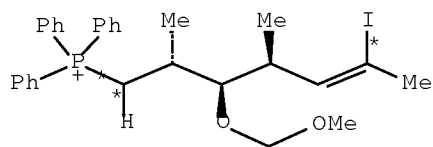
NTE BBN related byproducts were obtained in 10% yield, Suzuki
coupling

RX(28) RCT AX 633293-75-1
RGT CC 84-58-2 DDQ
PRO CO 633293-76-2
SOL 7732-18-5 Water, 75-09-2 CH2Cl2
CON 0 - room temperature deg C

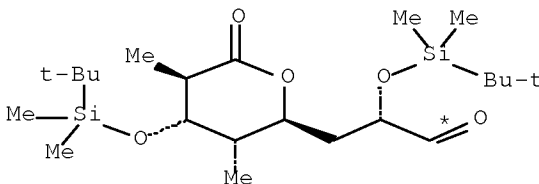
RX(29) RCT CO 633293-76-2, CP 3019-71-4
RGT CR 1344-28-1 Al2O3
PRO CQ 633293-93-3

RX(89) OF 354 COMPOSED OF RX(27), RX(11), RX(28), RX(29)

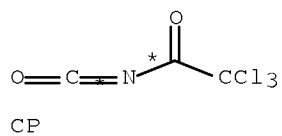
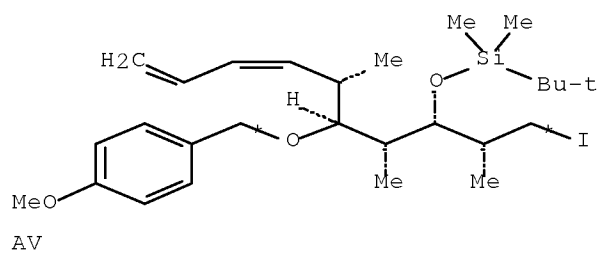
RX(89) CE + CN + AV + CP ==> CQ



CE

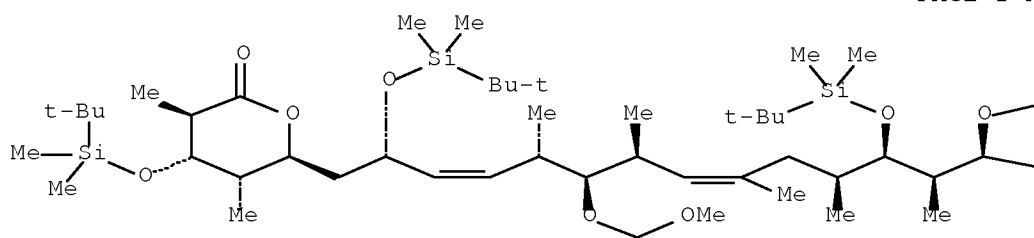


CN

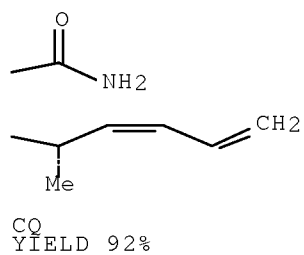


4
 STEPS

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RX(27)	RCT	CE 850211-72-2, CN 252342-51-1
	RGT	CA 1070-89-9 (Me3Si)2N.Na
	PRO	AW 850211-74-4
	CON	-78 deg C -> -10 deg C
	NTE	stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) -78 deg C
SUBSTAGE(3) -78 deg C -> room temperature
SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AW 850211-74-4
RGT BA 534-17-8 Cs2CO3
CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

PRO AX 633293-75-1

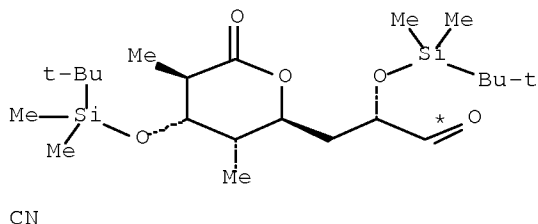
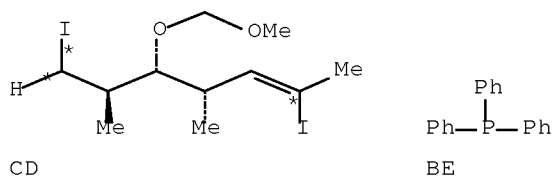
NTE BBN related byproducts were obtained in 10% yield, Suzuki
coupling

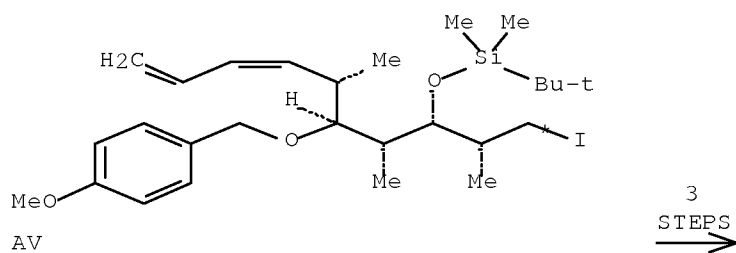
RX(28) RCT AX 633293-75-1
RGT CC 84-58-2 DDQ
PRO CO 633293-76-2
SOL 7732-18-5 Water, 75-09-2 CH2Cl2
CON 0 - room temperature deg C

RX(29) RCT CO 633293-76-2, CP 3019-71-4
RGT CR 1344-28-1 Al2O3
PRO CQ 633293-93-3

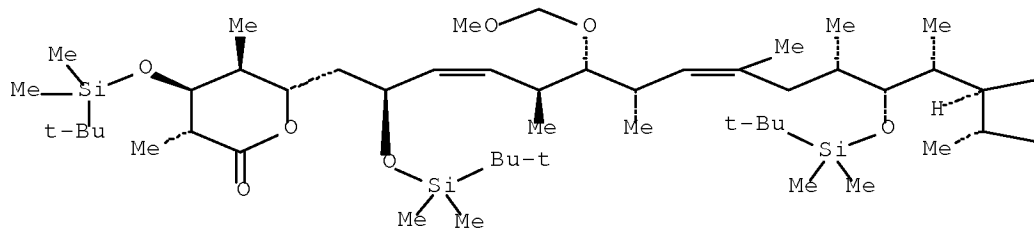
RX(115) OF 354 COMPOSED OF RX(23), RX(27), RX(11)

RX(115) CD + BE + CN + AV ==> AX

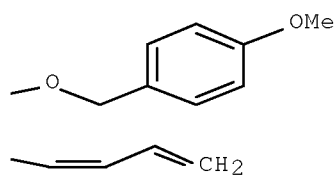




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AX
 YIELD 50%

RX(23)	RCT	CD 850211-71-1, BE 603-35-0
	PRO	CE 850211-72-2
	CON	100 deg C
	NTE	yield over 11 steps starting from Roche's ester = 27%
RX(27)	RCT	CE 850211-72-2, CN 252342-51-1
	RGT	CA 1070-89-9 (Me ₃ Si) ₂ N.Na
	PRO	AW 850211-74-4
	CON	-78 deg C -> -10 deg C
	NTE	stereoselective, Wittig coupling, yield over 13 steps = 20%
RX(11)	RCT	AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
 SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
 Pentane
 CON SUBSTAGE(1) room temperature -> -78 deg C
 SUBSTAGE(2) -78 deg C
 SUBSTAGE(3) -78 deg C -> room temperature
 SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

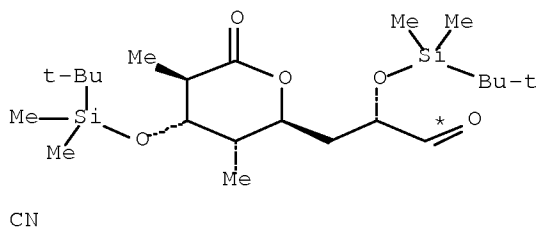
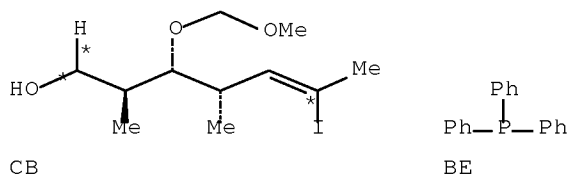
RCT AW 850211-74-4
 RGT BA 534-17-8 Cs2CO3
 CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

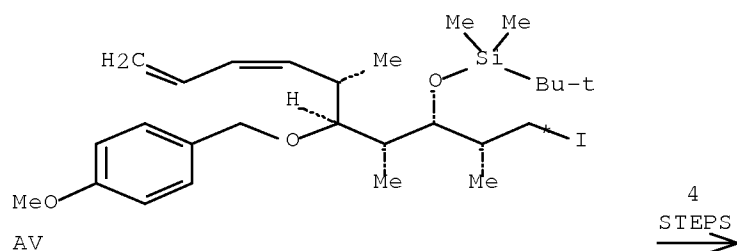
PRO AX 633293-75-1

NTE BBN related byproducts were obtained in 10% yield, Suzuki
 coupling

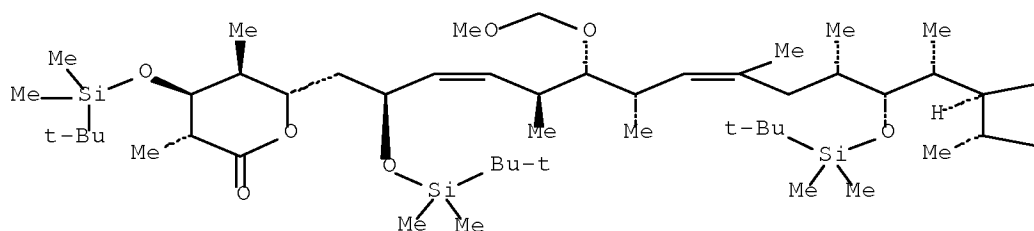
RX(116) OF 354 COMPOSED OF RX(22), RX(23), RX(27), RX(11)

RX(116) CB + BE + CN + AV ==> AX

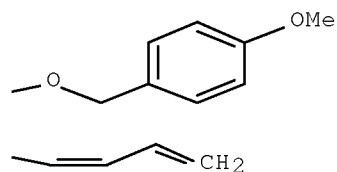




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AX
 YIELD 50%

RX(22)	RCT	CB 850211-70-0
	RGT	BE 603-35-0 PPh ₃ , BF 7553-56-2 I ₂ , BG 288-32-4 1H-Imidazole
	PRO	CD 850211-71-1
RX(23)	RCT	CD 850211-71-1, BE 603-35-0
	PRO	CE 850211-72-2
	CON	100 deg C
	NTE	yield over 11 steps starting from Roche's ester = 27%
RX(27)	RCT	CE 850211-72-2, CN 252342-51-1
	RGT	CA 1070-89-9 (Me ₃ Si) ₂ N.Na
	PRO	AW 850211-74-4
	CON	-78 deg C -> -10 deg C
	NTE	stereoselective, Wittig coupling, yield over 13 steps = 20%
RX(11)	RCT	AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
 SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
 Pentane
 CON SUBSTAGE(1) room temperature -> -78 deg C
 SUBSTAGE(2) -78 deg C
 SUBSTAGE(3) -78 deg C -> room temperature
 SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

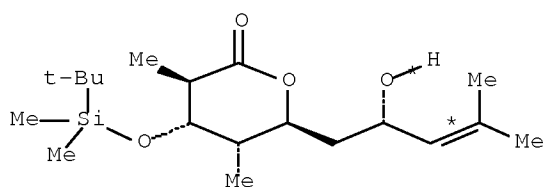
RCT AW 850211-74-4
 RGT BA 534-17-8 Cs2CO3
 CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

PRO AX 633293-75-1

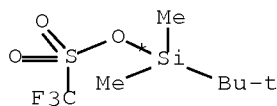
NTE BBN related byproducts were obtained in 10% yield, Suzuki
 coupling

RX(121) OF 354 COMPOSED OF RX(26), RX(27), RX(11)

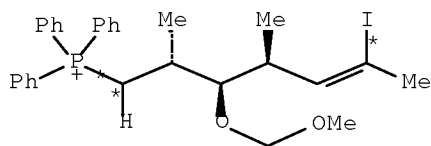
RX(121) CM + L + CE + AV ==> AX



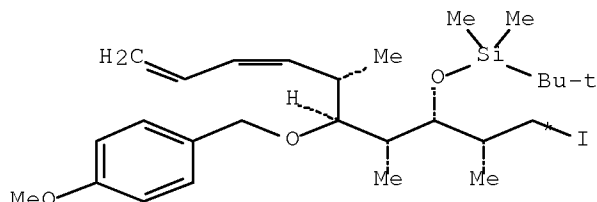
CM



L



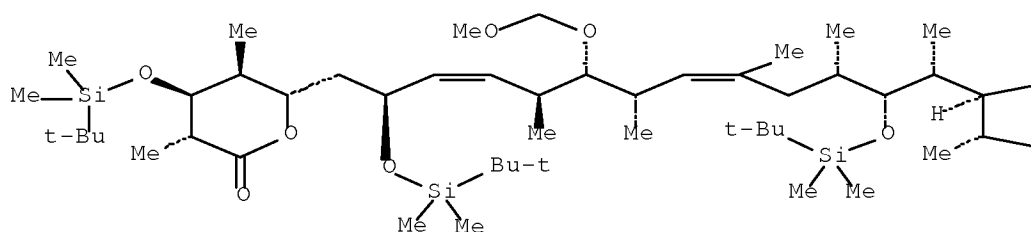
CE



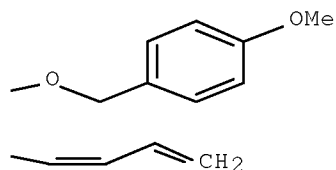
AV

3
STEPS
→

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AX
YIELD 50%

RX(26) RCT CM 256920-77-1, L 69739-34-0

STAGE(1)

SOL 75-09-2 CH₂Cl₂

STAGE(2)

RGT AJ 10028-15-6 Ozone

SOL 75-09-2 CH₂Cl₂

STAGE(3)

RGT BE 603-35-0 PPh₃

PRO CN 252342-51-1

NTE yield over 12 steps starting from Roche's ester = 33%

RX(27) RCT CE 850211-72-2, CN 252342-51-1

RGT CA 1070-89-9 (Me₃Si)₂N.Na

PRO AW 850211-74-4

CON -78 deg C -> -10 deg C

NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) -78 deg C
SUBSTAGE(3) -78 deg C -> room temperature
SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

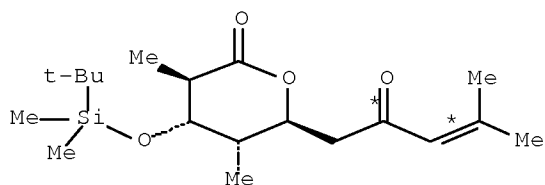
RCT AW 850211-74-4
RGT BA 534-17-8 Cs2CO3
CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

PRO AX 633293-75-1

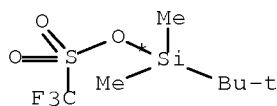
NTE BBN related byproducts were obtained in 10% yield, Suzuki
coupling

RX(122) OF 354 COMPOSED OF RX(33), RX(26), RX(27), RX(11)

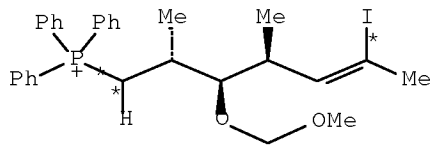
RX(122) CJ + L + CE + AV ==> AX



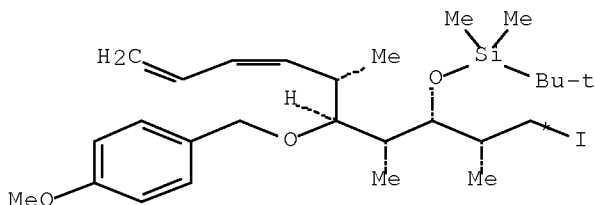
CJ



L



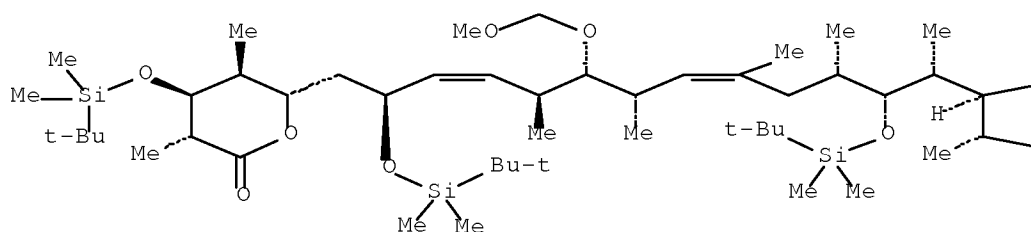
CE



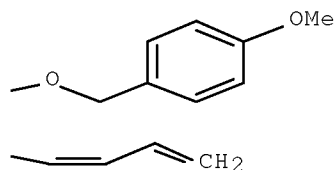
AV

4
STEPS
→

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AX
YIELD 50%

RX(33) RCT CJ 252342-43-1
RGT CW 54575-49-4 K Selectride
PRO CM 256920-77-1
SOL 109-99-9 THF, 108-88-3 PhMe
NTE stereoselective, ratio of diastereomers = 9:1

RX(26) RCT CM 256920-77-1, L 69739-34-0

STAGE(1)
SOL 75-09-2 CH2Cl2

STAGE(2)
RGT AJ 10028-15-6 Ozone
SOL 75-09-2 CH2Cl2

STAGE(3)
RGT BE 603-35-0 PPh3

PRO CN 252342-51-1
NTE yield over 12 steps starting from Roche's ester = 33%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
 RGT CA 1070-89-9 (Me3Si)2N.Na
 PRO AW 850211-74-4
 CON -78 deg C -> -10 deg C
 NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
 SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0 Pentane
 CON SUBSTAGE(1) room temperature -> -78 deg C
 SUBSTAGE(2) -78 deg C
 SUBSTAGE(3) -78 deg C -> room temperature
 SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

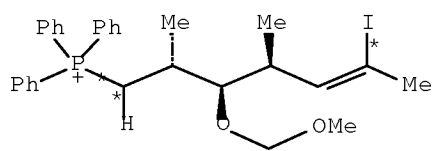
RCT AW 850211-74-4
 RGT BA 534-17-8 Cs2CO3
 CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

PRO AX 633293-75-1

NTE BBN related byproducts were obtained in 10% yield, Suzuki coupling

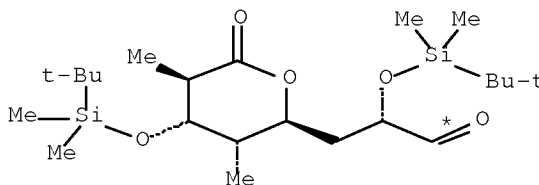
RX(123) OF 354 COMPOSED OF RX(27), RX(11), RX(28)

RX(123) CE + CN + AV ==> CO

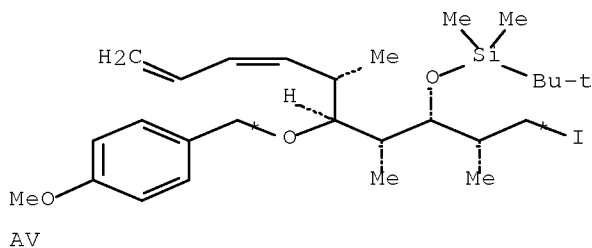


● I⁻

CE



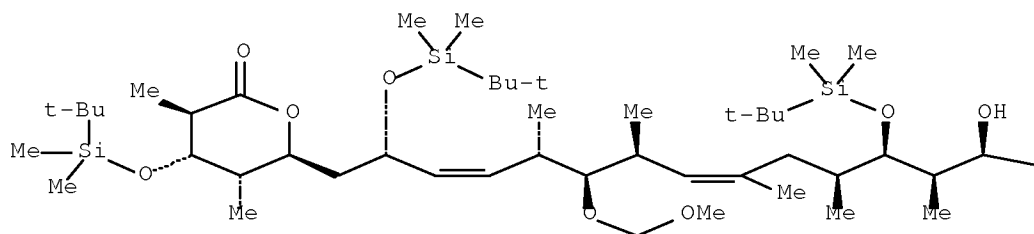
CN



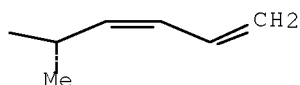
AV

3
STEPS
→

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PAGE 1-B



CO
YIELD 91%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
RGT CA 1070-89-9 (Me₃Si)₂N.Na
PRO AW 850211-74-4
CON -78 deg C -> -10 deg C
NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
SOL 60-29-7 Et₂O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) -78 deg C
SUBSTAGE(3) -78 deg C -> room temperature
SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AW 850211-74-4
RGT BA 534-17-8 Cs₂CO₃
CAT 603-32-7 Ph₃As, 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-

SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

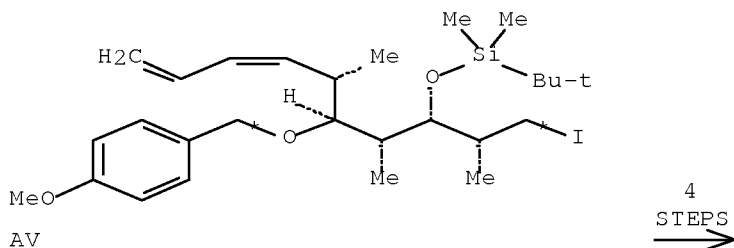
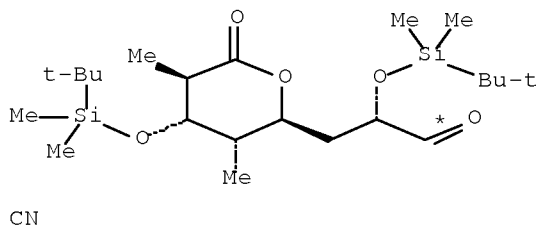
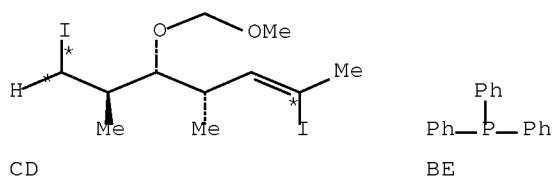
PRO AX 633293-75-1

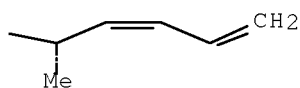
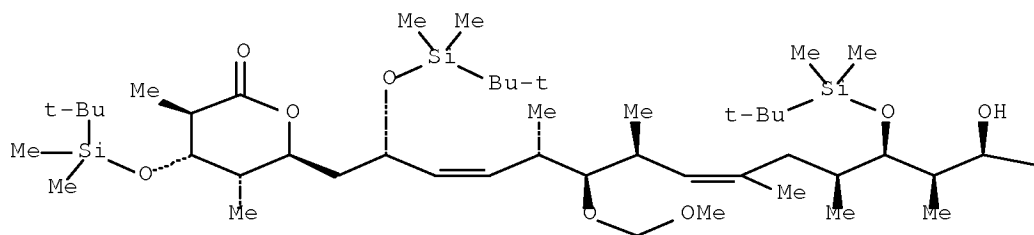
NTE BBN related byproducts were obtained in 10% yield, Suzuki coupling

RX(28) RCT AX 633293-75-1
 RGT CC 84-58-2 DDQ
 PRO CO 633293-76-2
 SOL 7732-18-5 Water, 75-09-2 CH2Cl2
 CON 0 - room temperature deg C

RX(124) OF 354 COMPOSED OF RX(23), RX(27), RX(11), RX(28)

RX(124) CD + BE + CN + AV ==> CO





CO
YIELD 91%

RX(23) RCT CD 850211-71-1, BE 603-35-0
 PRO CE 850211-72-2
 CON 100 deg C
 NTE yield over 11 steps starting from Roche's ester = 27%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
 RGT CA 1070-89-9 (Me₃Si)₂N.Na
 PRO AW 850211-74-4
 CON -78 deg C -> -10 deg C
 NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
 SOL 60-29-7 Et₂O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
 Pentane
 CON SUBSTAGE(1) room temperature -> -78 deg C
 SUBSTAGE(2) -78 deg C
 SUBSTAGE(3) -78 deg C -> room temperature
 SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AW 850211-74-4
 RGT BA 534-17-8 Cs₂CO₃
 CAT 603-32-7 Ph₃As, 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
 (SP-4-2)-

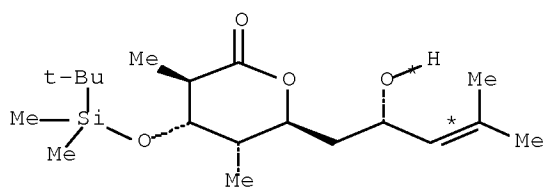
SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

PRO AX 633293-75-1

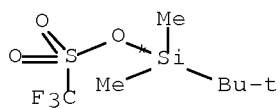
NTE BBN related byproducts were obtained in 10% yield, Suzuki coupling

RX(28) RCT AX 633293-75-1
 RGT CC 84-58-2 DDQ
 PRO CO 633293-76-2
 SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
 CON 0 - room temperature deg C

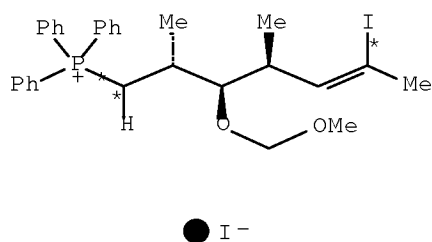
RX(125) OF 354 COMPOSED OF RX(26), RX(27), RX(11), RX(28)
 RX(125) CM + L + CE + AV ==> CO



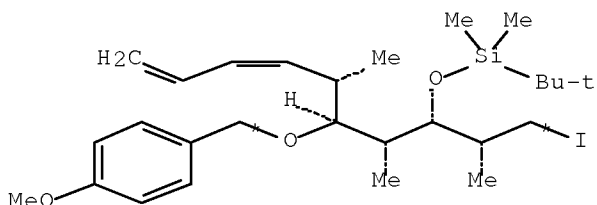
CM



L

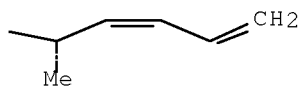
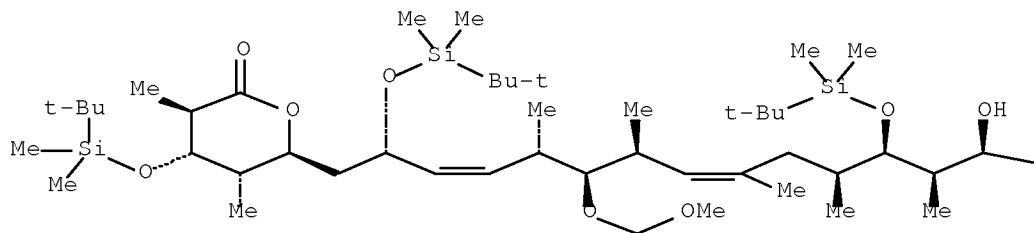


CE



AV

4
 STEPS
 →



CO
YIELD 91%

RX(26) RCT CM 256920-77-1, L 69739-34-0

STAGE(1)

SOL 75-09-2 CH₂Cl₂

STAGE(2)

RGT AJ 10028-15-6 Ozone

SOL 75-09-2 CH₂Cl₂

STAGE(3)

RGT BE 603-35-0 PPh₃

PRO CN 252342-51-1

NTE yield over 12 steps starting from Roche's ester = 33%

RX(27) RCT CE 850211-72-2, CN 252342-51-1

RGT CA 1070-89-9 (Me₃Si)₂N.Na

PRO AW 850211-74-4

CON -78 deg C -> -10 deg C

NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi

SOL 60-29-7 Et₂O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0 Pentane

CON SUBSTAGE(1) room temperature -> -78 deg C

SUBSTAGE(2) -78 deg C

SUBSTAGE(3) -78 deg C -> room temperature
SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

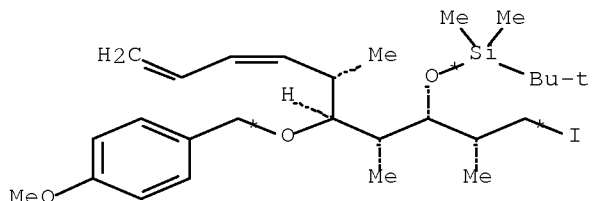
RCT AW 850211-74-4
RGT BA 534-17-8 Cs2CO3
CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

PRO AX 633293-75-1
NTE BBN related byproducts were obtained in 10% yield, Suzuki
coupling

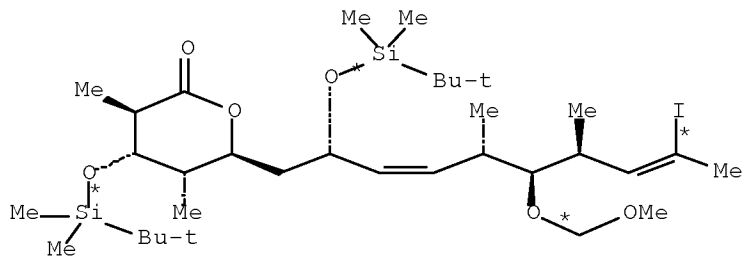
RX(28) RCT AX 633293-75-1
RGT CC 84-58-2 DDQ
PRO CO 633293-76-2
SOL 7732-18-5 Water, 75-09-2 CH2Cl2
CON 0 - room temperature deg C

RX(127) OF 354 COMPOSED OF RX(11), RX(28), RX(29), RX(30)

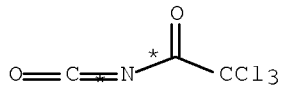
RX(127) AV + AW + CP ==> CS



AV

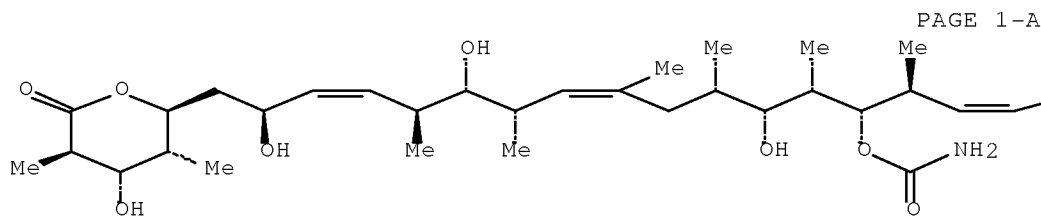


AW



CP

4
STEPS
→



PAGE 1-B

CS
YIELD 95%

RX(11) RCT AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) -78 deg C
SUBSTAGE(3) -78 deg C -> room temperature
SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AW 850211-74-4
RGT BA 534-17-8 Cs2CO3
CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

PRO AX 633293-75-1

NTE BBN related byproducts were obtained in 10% yield, Suzuki
coupling

RX(28) RCT AX 633293-75-1
RGT CC 84-58-2 DDQ
PRO CO 633293-76-2

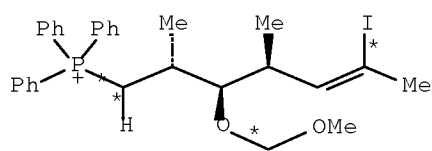
SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
 CON 0 - room temperature deg C

RX(29) RCT CO 633293-76-2, CP 3019-71-4
 RGT CR 1344-28-1 Al₂O₃
 PRO CQ 633293-93-3

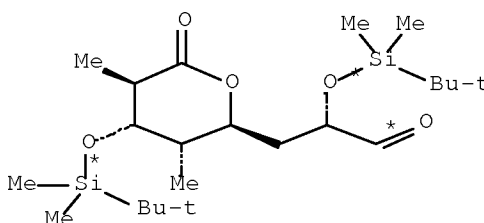
RX(30) RCT CQ 633293-93-3
 RGT CT 7647-01-0 HCl
 PRO CS 127943-53-7
 SOL 7732-18-5 Water, 67-56-1 MeOH
 NTE overall yield via iodine substituted pyran-2-one intermediate = 10%

RX(175) OF 354 COMPOSED OF RX(27), RX(11), RX(28), RX(29), RX(30)

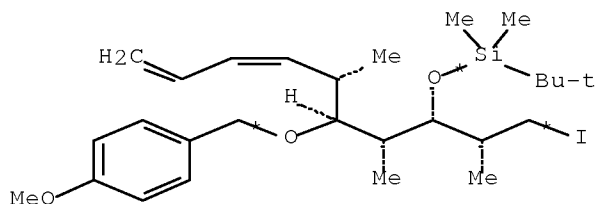
RX(175) CE + CN + AV + CP ==> CS



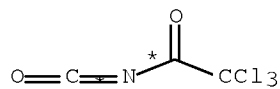
CE



CN

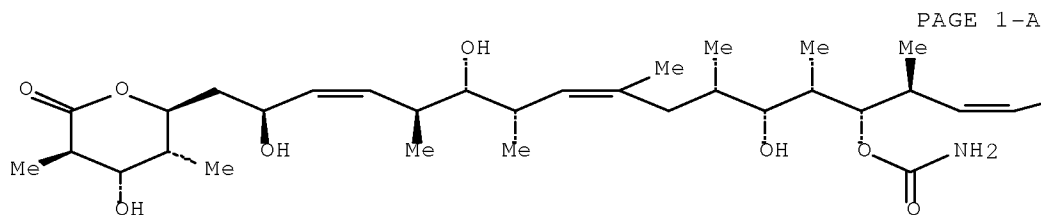


AV

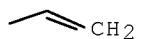


CP

5
 STEPS
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PAGE 1-B



CS
YIELD 95%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
RGT CA 1070-89-9 (Me3Si)2N.Na
PRO AW 850211-74-4
CON -78 deg C -> -10 deg C
NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) -78 deg C
SUBSTAGE(3) -78 deg C -> room temperature
SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AW 850211-74-4
RGT BA 534-17-8 Cs2CO3
CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

PRO AX 633293-75-1

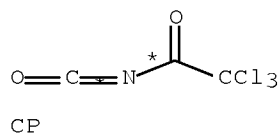
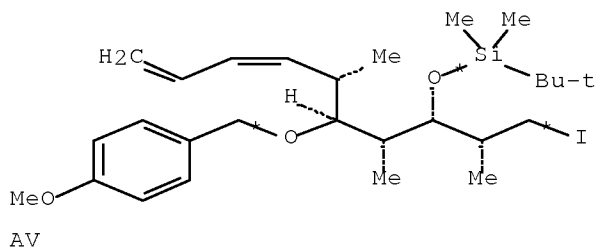
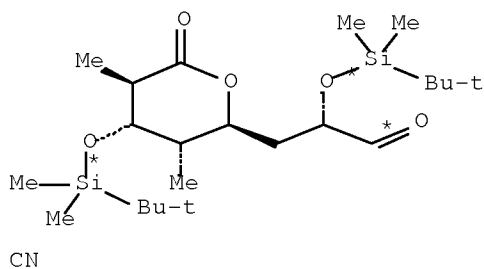
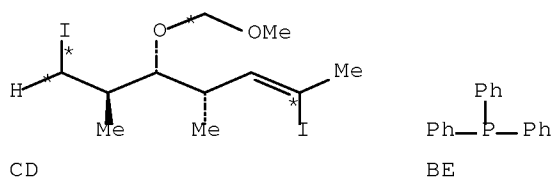
NTE BBN related byproducts were obtained in 10% yield, Suzuki
coupling

RX(28) RCT AX 633293-75-1
RGT CC 84-58-2 DDQ
PRO CO 633293-76-2
SOL 7732-18-5 Water, 75-09-2 CH2Cl2
CON 0 - room temperature deg C

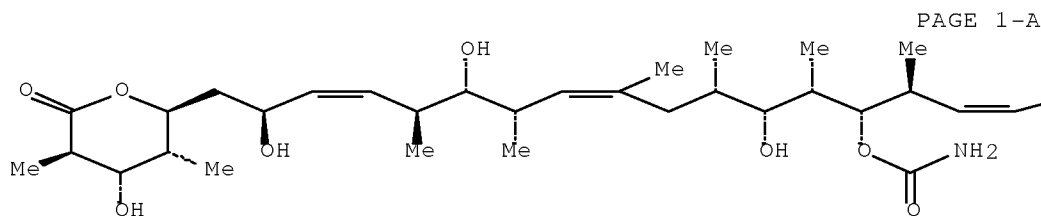
RX(29) RCT CO 633293-76-2, CP 3019-71-4
 RGT CR 1344-28-1 Al2O3
 PRO CQ 633293-93-3

RX(30) RCT CQ 633293-93-3
 RGT CT 7647-01-0 HCl
 PRO CS 127943-53-7
 SOL 7732-18-5 Water, 67-56-1 MeOH
 NTE overall yield via iodine substituted pyran-2-one intermediate = 10%

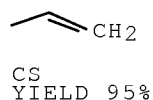
RX(178) OF 354 COMPOSED OF RX(23), RX(27), RX(11), RX(28), RX(29), RX(30)
 RX(178) CD + BE + CN + AV + CP ==> CS



6
STEPS
→



PAGE 1-B



RX(23) RCT CD 850211-71-1, BE 603-35-0
 PRO CE 850211-72-2
 CON 100 deg C
 NTE yield over 11 steps starting from Roche's ester = 27%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
 RGT CA 1070-89-9 (Me3Si)2N.Na
 PRO AW 850211-74-4
 CON -78 deg C -> -10 deg C
 NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)
 RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
 SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0 Pentane
 CON SUBSTAGE(1) room temperature -> -78 deg C
 SUBSTAGE(2) -78 deg C
 SUBSTAGE(3) -78 deg C -> room temperature
 SUBSTAGE(4) 1 hour, room temperature

STAGE(2)
 RCT AW 850211-74-4
 RGT BA 534-17-8 Cs2CO3
 CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
 (SP-4-2)-

SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

PRO AX 633293-75-1

NTE BBN related byproducts were obtained in 10% yield, Suzuki coupling

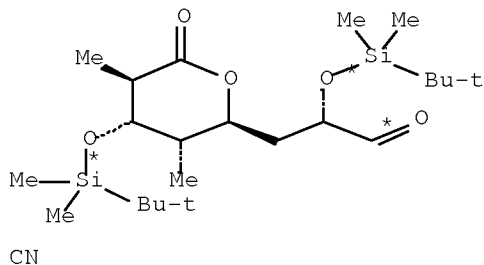
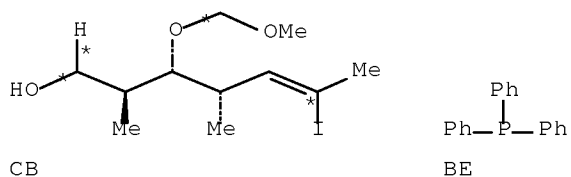
RX(28) RCT AX 633293-75-1
 RGT CC 84-58-2 DDQ
 PRO CO 633293-76-2
 SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
 CON 0 - room temperature deg C

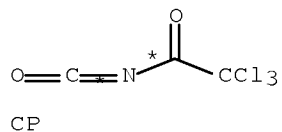
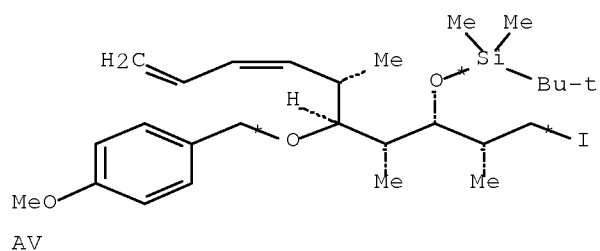
RX(29) RCT CO 633293-76-2, CP 3019-71-4
 RGT CR 1344-28-1 Al₂O₃
 PRO CQ 633293-93-3

RX(30) RCT CQ 633293-93-3
 RGT CT 7647-01-0 HCl
 PRO CS 127943-53-7
 SOL 7732-18-5 Water, 67-56-1 MeOH
 NTE overall yield via iodine substituted pyran-2-one intermediate = 10%

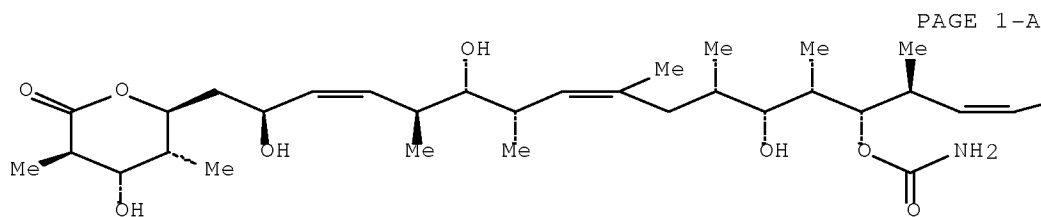
RX(179) OF 354 COMPOSED OF RX(22), RX(23), RX(27), RX(11), RX(28), RX(29),
 RX(30)

RX(179) CB + BE + CN + AV + CP ==> CS

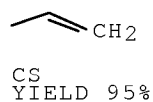




7
 STEPS
 →



PAGE 1-B



RX(22)	RCT	CB 850211-70-0
	RGT	BE 603-35-0 PPh3, BF 7553-56-2 I2, BG 288-32-4 1H-Imidazole
	PRO	CD 850211-71-1
RX(23)	RCT	CD 850211-71-1, BE 603-35-0
	PRO	CE 850211-72-2
	CON	100 deg C
	NTE	yield over 11 steps starting from Roche's ester = 27%
RX(27)	RCT	CE 850211-72-2, CN 252342-51-1
	RGT	CA 1070-89-9 (Me3Si)2N.Na
	PRO	AW 850211-74-4
	CON	-78 deg C -> -10 deg C

NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) -78 deg C
SUBSTAGE(3) -78 deg C -> room temperature
SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AW 850211-74-4
RGT BA 534-17-8 Cs2CO3
CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

PRO AX 633293-75-1

NTE BBN related byproducts were obtained in 10% yield, Suzuki
coupling

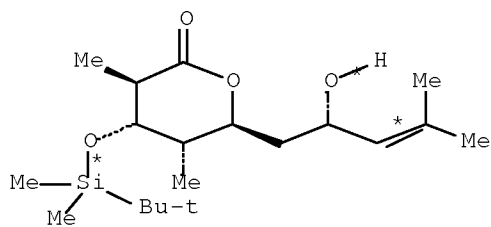
RX(28) RCT AX 633293-75-1
RGT CC 84-58-2 DDQ
PRO CO 633293-76-2
SOL 7732-18-5 Water, 75-09-2 CH2Cl2
CON 0 - room temperature deg C

RX(29) RCT CO 633293-76-2, CP 3019-71-4
RGT CR 1344-28-1 Al2O3
PRO CQ 633293-93-3

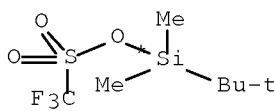
RX(30) RCT CQ 633293-93-3
RGT CT 7647-01-0 HCl
PRO CS 127943-53-7
SOL 7732-18-5 Water, 67-56-1 MeOH
NTE overall yield via iodine substituted pyran-2-one intermediate =
10%

RX(180) OF 354 COMPOSED OF RX(26), RX(27), RX(11), RX(28), RX(29), RX(30)

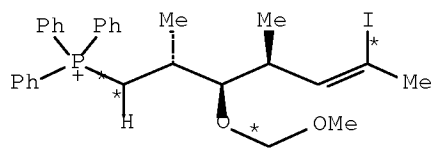
RX(180) CM + L + CE + AV + CP ==> CS



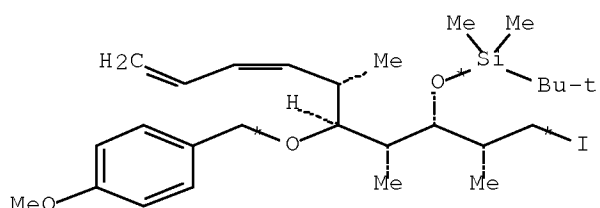
CM



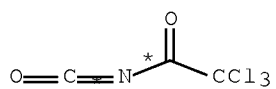
L



CE

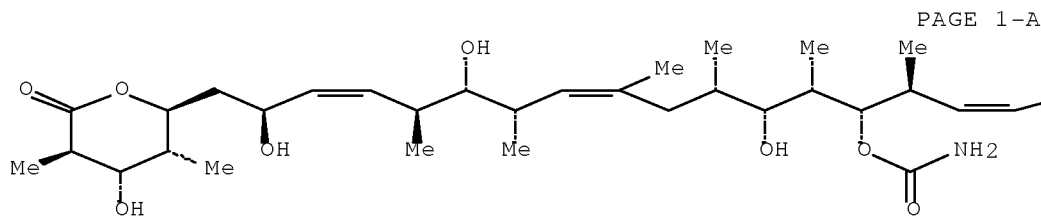


AV

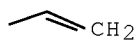


CP

6
STEPS
→



PAGE 1-B



CS
YIELD 95%

RX(26) RCT CM 256920-77-1, L 69739-34-0

STAGE(1)

SOL 75-09-2 CH2Cl2

STAGE(2)

RGT AJ 10028-15-6 Ozone
SOL 75-09-2 CH2Cl2

STAGE(3)

RGT BE 603-35-0 PPh3

PRO CN 252342-51-1

NTE yield over 12 steps starting from Roche's ester = 33%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
RGT CA 1070-89-9 (Me3Si)2N.Na
PRO AW 850211-74-4
CON -78 deg C -> -10 deg C
NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi

SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane

CON SUBSTAGE(1) room temperature -> -78 deg C

SUBSTAGE(2) -78 deg C

SUBSTAGE(3) -78 deg C -> room temperature

SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AW 850211-74-4

RGT BA 534-17-8 Cs2CO3

CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-

SOL 7732-18-5 Water, 68-12-2 DMF

CON 20 hours, room temperature

PRO AX 633293-75-1

NTE BBN related byproducts were obtained in 10% yield, Suzuki
coupling

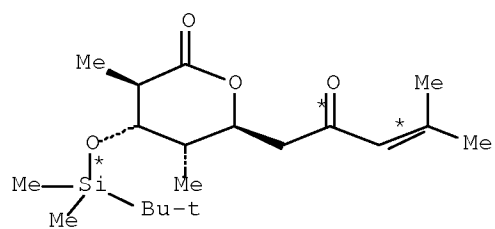
RX(28) RCT AX 633293-75-1
RGT CC 84-58-2 DDQ
PRO CO 633293-76-2
SOL 7732-18-5 Water, 75-09-2 CH2Cl2
CON 0 - room temperature deg C

RX(29) RCT CO 633293-76-2, CP 3019-71-4
RGT CR 1344-28-1 Al2O3
PRO CQ 633293-93-3

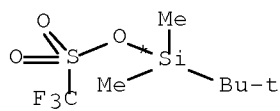
RX(30) RCT CQ 633293-93-3
RGT CT 7647-01-0 HCl
PRO CS 127943-53-7
SOL 7732-18-5 Water, 67-56-1 MeOH
NTE overall yield via iodine substituted pyran-2-one intermediate =
10%

RX(181) OF 354 COMPOSED OF RX(33), RX(26), RX(27), RX(11), RX(28), RX(29),
RX(30)

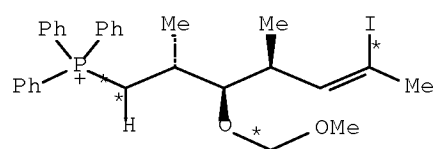
RX(181) CJ + L + CE + AV + CP ==> CS



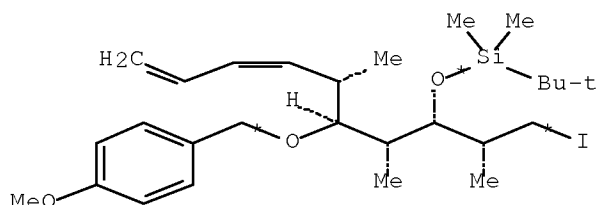
CJ



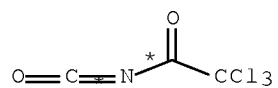
L



CE



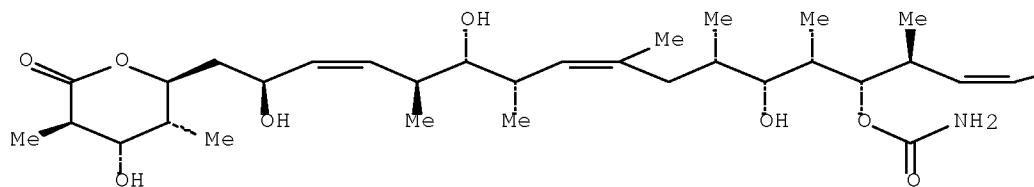
AV

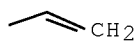


CP

7
STEPS
→

PAGE 1-A





CS
YIELD 95%

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RX(33)  RCT  CJ 252342-43-1
        RGT  CW 54575-49-4 K Selectride
        PRO  CM 256920-77-1
        SOL  109-99-9 THF, 108-88-3 PhMe
        NTE  stereoselective, ratio of diastereomers = 9:1

RX(26)  RCT  CM 256920-77-1, L 69739-34-0

        STAGE(1)
          SOL  75-09-2 CH2Cl2

        STAGE(2)
          RGT  AJ 10028-15-6 Ozone
          SOL  75-09-2 CH2Cl2

        STAGE(3)
          RGT  BE 603-35-0 PPh3

        PRO  CN 252342-51-1
        NTE  yield over 12 steps starting from Roche's ester = 33%

RX(27)  RCT  CE 850211-72-2, CN 252342-51-1
        RGT  CA 1070-89-9 (Me3Si)2N.Na
        PRO  AW 850211-74-4
        CON  -78 deg C -> -10 deg C
        NTE  stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11)  RCT  AV 850211-69-7

        STAGE(1)
          RGT  AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
          SOL  60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
                Pentane
          CON  SUBSTAGE(1) room temperature -> -78 deg C
                SUBSTAGE(2) -78 deg C
                SUBSTAGE(3) -78 deg C -> room temperature
                SUBSTAGE(4) 1 hour, room temperature

        STAGE(2)
          RCT  AW 850211-74-4
          RGT  BA 534-17-8 Cs2CO3
          CAT  603-32-7 Ph3As, 72287-26-4 Palladium,
                [1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
                (SP-4-2)-
          SOL  7732-18-5 Water, 68-12-2 DMF
          CON  20 hours, room temperature

        PRO  AX 633293-75-1

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NTE BBN related byproducts were obtained in 10% yield, Suzuki coupling

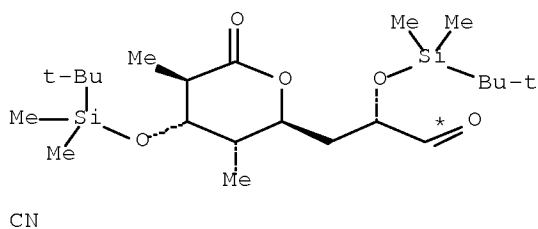
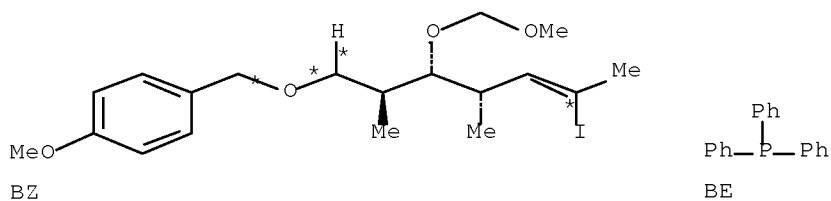
RX(28) RCT AX 633293-75-1
 RGT CC 84-58-2 DDQ
 PRO CO 633293-76-2
 SOL 7732-18-5 Water, 75-09-2 CH2Cl2
 CON 0 - room temperature deg C

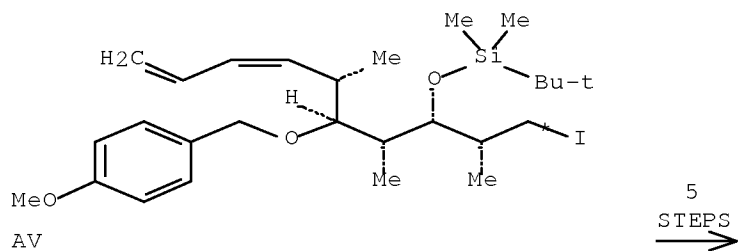
RX(29) RCT CO 633293-76-2, CP 3019-71-4
 RGT CR 1344-28-1 Al2O3
 PRO CQ 633293-93-3

RX(30) RCT CQ 633293-93-3
 RGT CT 7647-01-0 HCl
 PRO CS 127943-53-7
 SOL 7732-18-5 Water, 67-56-1 MeOH
 NTE overall yield via iodine substituted pyran-2-one intermediate = 10%

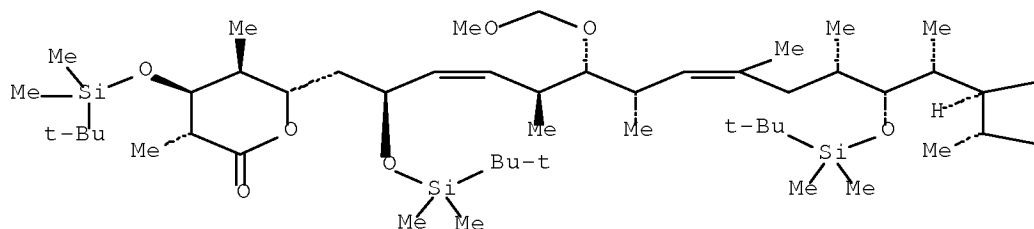
RX(222) OF 354 COMPOSED OF RX(21), RX(22), RX(23), RX(27), RX(11)

RX(222) BZ + BE + CN + AV ==> AX

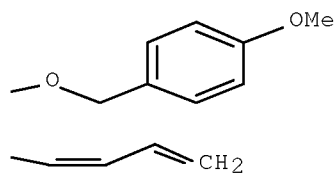




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AX
 YIELD 50%

RX(21)	RCT	BZ 633294-02-7
	RGT	CC 84-58-2 DDQ
	PRO	CB 850211-70-0
	SOL	7732-18-5 Water
RX(22)	RCT	CB 850211-70-0
	RGT	BE 603-35-0 PPh ₃ , BF 7553-56-2 I ₂ , BG 288-32-4 1H-Imidazole
	PRO	CD 850211-71-1
RX(23)	RCT	CD 850211-71-1, BE 603-35-0
	PRO	CE 850211-72-2
	CON	100 deg C
	NTE	yield over 11 steps starting from Roche's ester = 27%
RX(27)	RCT	CE 850211-72-2, CN 252342-51-1
	RGT	CA 1070-89-9 (Me ₃ Si) ₂ N.Na

PRO AW 850211-74-4
 CON -78 deg C -> -10 deg C
 NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
 SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
 Pentane
 CON SUBSTAGE(1) room temperature -> -78 deg C
 SUBSTAGE(2) -78 deg C
 SUBSTAGE(3) -78 deg C -> room temperature
 SUBSTAGE(4) 1 hour, room temperature

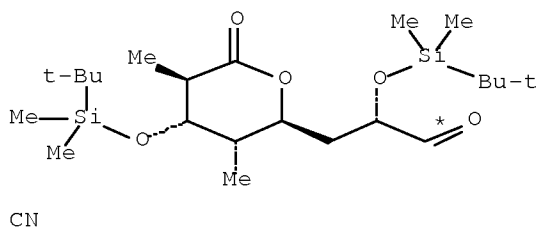
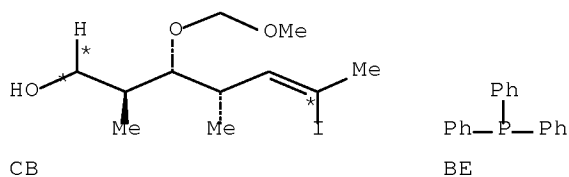
STAGE(2)

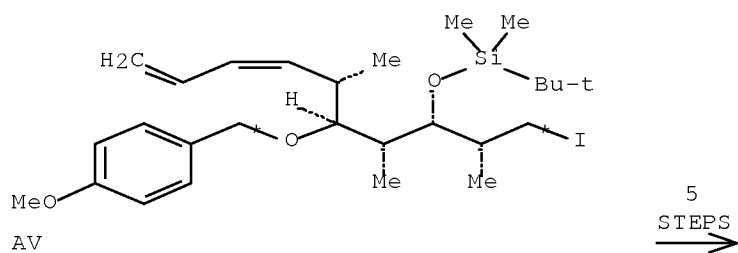
RCT AW 850211-74-4
 RGT BA 534-17-8 Cs2CO3
 CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

PRO AX 633293-75-1

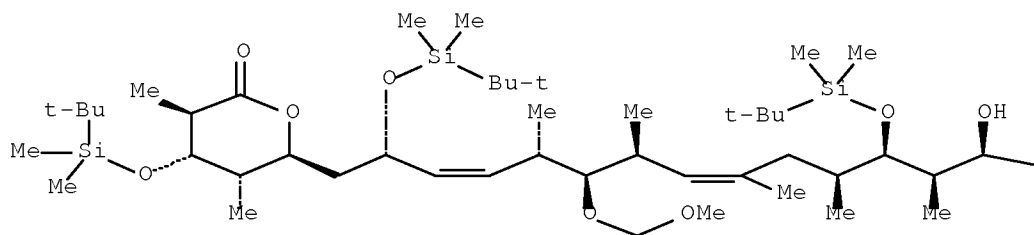
NTE BBN related byproducts were obtained in 10% yield, Suzuki
 coupling

RX(226) OF 354 COMPOSED OF RX(22), RX(23), RX(27), RX(11), RX(28)
 RX(226) CB + BE + CN + AV ==> CO

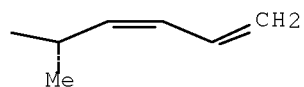




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CO
YIELD 91%

RX(22)	RCT	CB 850211-70-0
	RGT	BE 603-35-0 PPh ₃ , BF 7553-56-2 I ₂ , BG 288-32-4 1H-Imidazole
	PRO	CD 850211-71-1
RX(23)	RCT	CD 850211-71-1, BE 603-35-0
	PRO	CE 850211-72-2
	CON	100 deg C
	NTE	yield over 11 steps starting from Roche's ester = 27%
RX(27)	RCT	CE 850211-72-2, CN 252342-51-1
	RGT	CA 1070-89-9 (Me ₃ Si) ₂ N.Na
	PRO	AW 850211-74-4
	CON	-78 deg C → -10 deg C
	NTE	stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) -78 deg C
SUBSTAGE(3) -78 deg C -> room temperature
SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

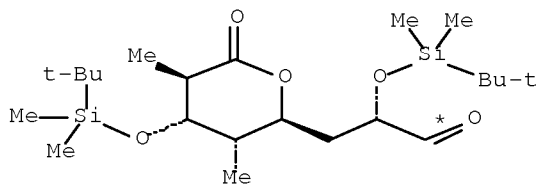
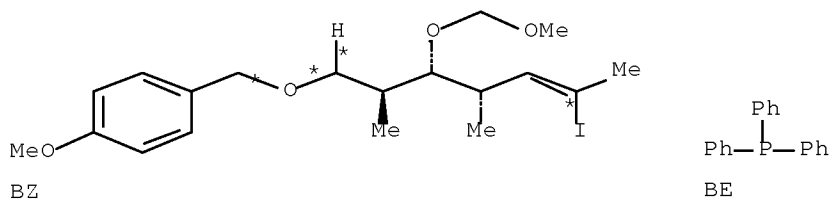
RCT AW 850211-74-4
RGT BA 534-17-8 Cs2CO3
CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

PRO AX 633293-75-1

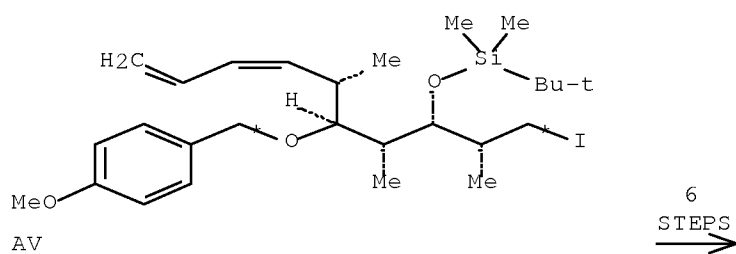
NTE BBN related byproducts were obtained in 10% yield, Suzuki
coupling

RX(28) RCT AX 633293-75-1
RGT CC 84-58-2 DDQ
PRO CO 633293-76-2
SOL 7732-18-5 Water, 75-09-2 CH2Cl2
CON 0 - room temperature deg C

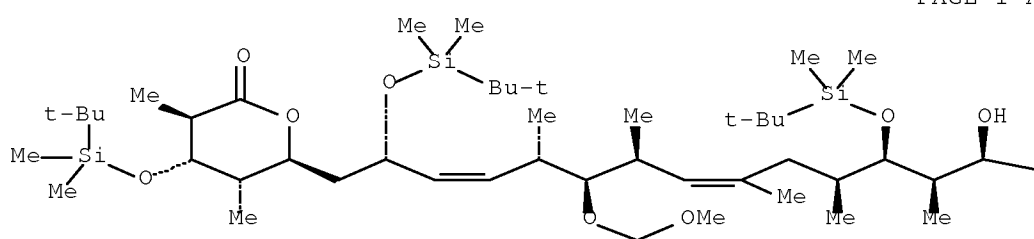
RX(227) OF 354 COMPOSED OF RX(21), RX(22), RX(23), RX(27), RX(11), RX(28)
RX(227) BZ + BE + CN + AV ==> CO



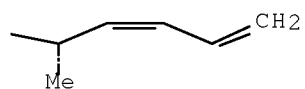
CN



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CO
YIELD 91%

RX(21)	RCT	BZ 633294-02-7
	RGT	CC 84-58-2 DDQ
	PRO	CB 850211-70-0
	SOL	7732-18-5 Water
RX(22)	RCT	CB 850211-70-0
	RGT	BE 603-35-0 PPh3, BF 7553-56-2 I2, BG 288-32-4 1H-Imidazole
	PRO	CD 850211-71-1
RX(23)	RCT	CD 850211-71-1, BE 603-35-0
	PRO	CE 850211-72-2
	CON	100 deg C

NTE yield over 11 steps starting from Roche's ester = 27%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
RGT CA 1070-89-9 (Me3Si)2N.Na
PRO AW 850211-74-4
CON -78 deg C -> -10 deg C
NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) -78 deg C
SUBSTAGE(3) -78 deg C -> room temperature
SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AW 850211-74-4
RGT BA 534-17-8 Cs2CO3
CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

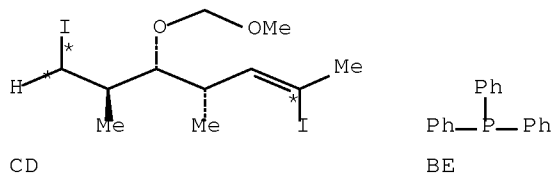
PRO AX 633293-75-1

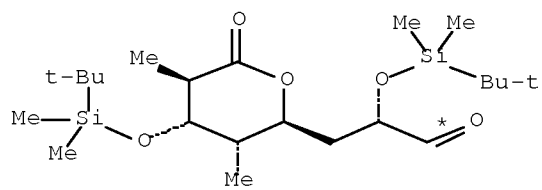
NTE BBN related byproducts were obtained in 10% yield, Suzuki
coupling

RX(28) RCT AX 633293-75-1
RGT CC 84-58-2 DDQ
PRO CO 633293-76-2
SOL 7732-18-5 Water, 75-09-2 CH2Cl2
CON 0 - room temperature deg C

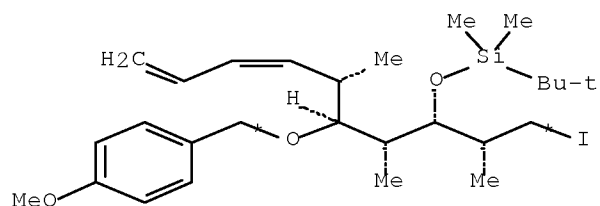
RX(230) OF 354 COMPOSED OF RX(23), RX(27), RX(11), RX(28), RX(29)

RX(230) CD + BE + CN + AV + CP ==> CQ

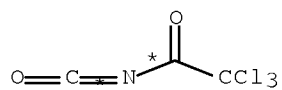




CN

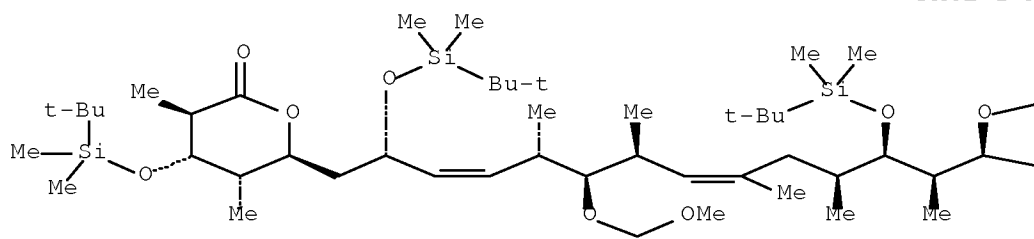


AV

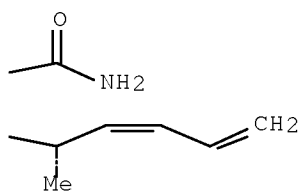


CP

5
STEPS
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CO
YIELD 92%

RX(23) RCT CD 850211-71-1, BE 603-35-0
 PRO CE 850211-72-2
 CON 100 deg C
 NTE yield over 11 steps starting from Roche's ester = 27%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
 RGT CA 1070-89-9 (Me3Si)2N.Na
 PRO AW 850211-74-4
 CON -78 deg C -> -10 deg C
 NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)
 RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
 SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0 Pentane
 CON SUBSTAGE(1) room temperature -> -78 deg C
 SUBSTAGE(2) -78 deg C
 SUBSTAGE(3) -78 deg C -> room temperature
 SUBSTAGE(4) 1 hour, room temperature

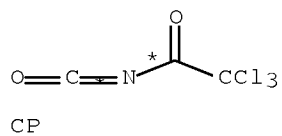
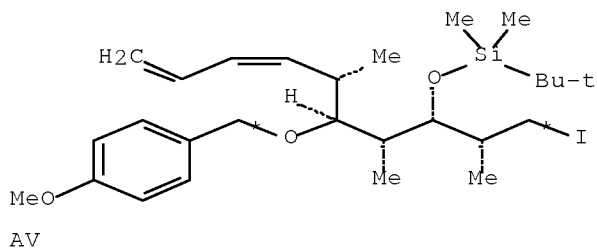
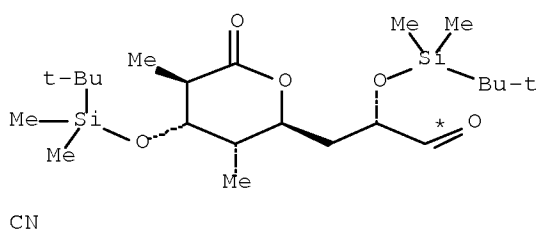
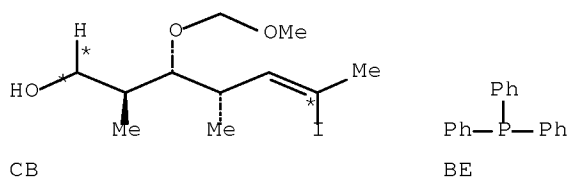
STAGE(2)
 RCT AW 850211-74-4
 RGT BA 534-17-8 Cs2CO3
 CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

PRO AX 633293-75-1
 NTE BBN related byproducts were obtained in 10% yield, Suzuki coupling

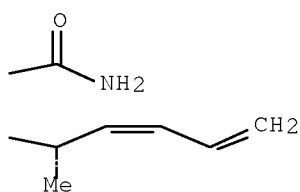
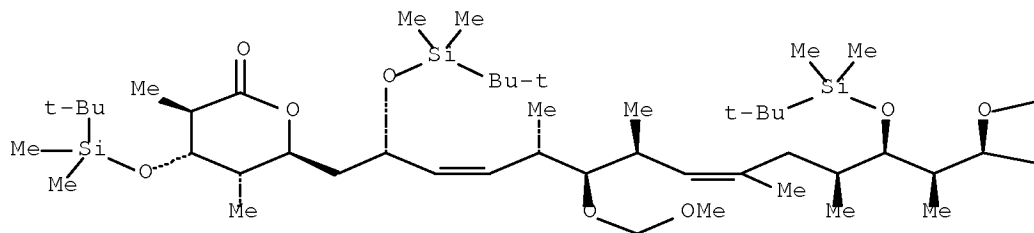
RX(28) RCT AX 633293-75-1
 RGT CC 84-58-2 DDQ
 PRO CO 633293-76-2
 SOL 7732-18-5 Water, 75-09-2 CH2Cl2
 CON 0 - room temperature deg C

RX(29) RCT CO 633293-76-2, CP 3019-71-4
 RGT CR 1344-28-1 Al2O3
 PRO CQ 633293-93-3

RX(231) OF 354 COMPOSED OF RX(22), RX(23), RX(27), RX(11), RX(28), RX(29)
 RX(231) CB + BE + CN + AV + CP ==> CQ



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 STEPS
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CO
YIELD 92%

RX(22) RCT CB 850211-70-0
RGT BE 603-35-0 PPh3, BF 7553-56-2 I2, BG 288-32-4 1H-Imidazole
PRO CD 850211-71-1

RX(23) RCT CD 850211-71-1, BE 603-35-0
PRO CE 850211-72-2
CON 100 deg C
NTE yield over 11 steps starting from Roche's ester = 27%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
RGT CA 1070-89-9 (Me3Si)2N.Na
PRO AW 850211-74-4
CON -78 deg C -> -10 deg C
NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0 Pentane
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) -78 deg C
SUBSTAGE(3) -78 deg C -> room temperature
SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AW 850211-74-4
RGT BA 534-17-8 Cs2CO3

CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

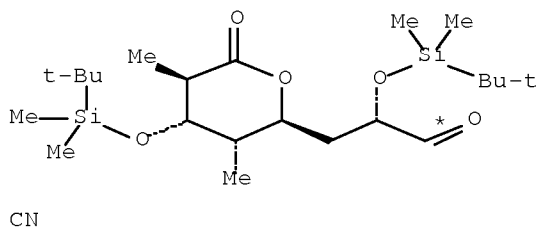
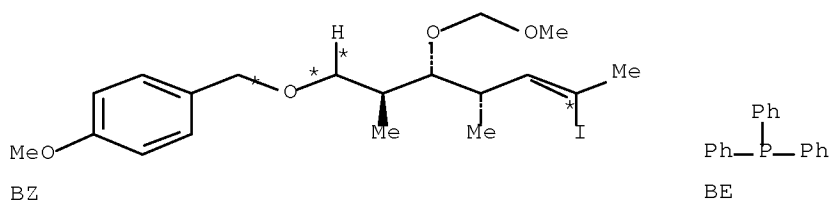
PRO AX 633293-75-1
 NTE BBN related byproducts were obtained in 10% yield, Suzuki
 coupling

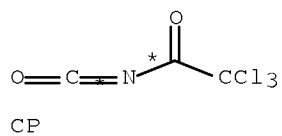
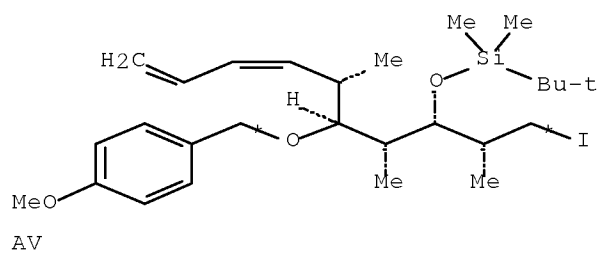
RX(28) RCT AX 633293-75-1
 RGT CC 84-58-2 DDQ
 PRO CO 633293-76-2
 SOL 7732-18-5 Water, 75-09-2 CH2Cl2
 CON 0 - room temperature deg C

RX(29) RCT CO 633293-76-2, CP 3019-71-4
 RGT CR 1344-28-1 Al2O3
 PRO CQ 633293-93-3

RX(232) OF 354 COMPOSED OF RX(21), RX(22), RX(23), RX(27), RX(11), RX(28),
 RX(29)

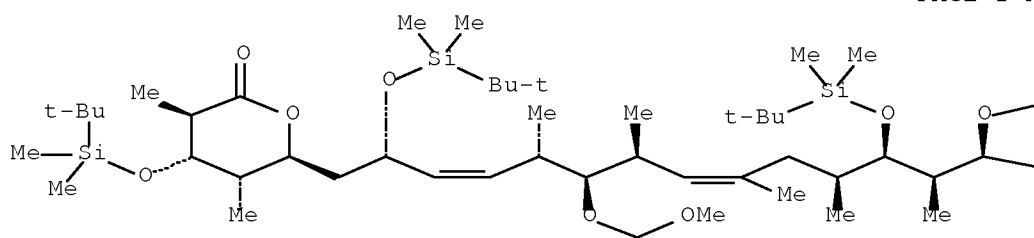
RX(232) BZ + BE + CN + AV + CP ==> CQ



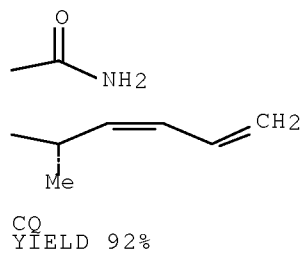


7
 STEPS
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RX(21) RCT BZ 633294-02-7
 RGT CC 84-58-2 DDQ
 PRO CB 850211-70-0
 SOL 7732-18-5 Water

RX(22) RCT CB 850211-70-0

RGT BE 603-35-0 PPh3, BF 7553-56-2 I2, BG 288-32-4 1H-Imidazole
PRO CD 850211-71-1

RX(23) RCT CD 850211-71-1, BE 603-35-0
PRO CE 850211-72-2
CON 100 deg C
NTE yield over 11 steps starting from Roche's ester = 27%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
RGT CA 1070-89-9 (Me3Si)2N.Na
PRO AW 850211-74-4
CON -78 deg C -> -10 deg C
NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) -78 deg C
SUBSTAGE(3) -78 deg C -> room temperature
SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AW 850211-74-4
RGT BA 534-17-8 Cs2CO3
CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

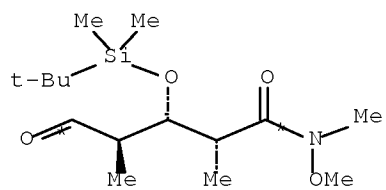
PRO AX 633293-75-1
NTE BBN related byproducts were obtained in 10% yield, Suzuki
coupling

RX(28) RCT AX 633293-75-1
RGT CC 84-58-2 DDQ
PRO CO 633293-76-2
SOL 7732-18-5 Water, 75-09-2 CH2Cl2
CON 0 - room temperature deg C

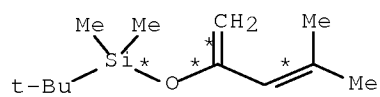
RX(29) RCT CO 633293-76-2, CP 3019-71-4
RGT CR 1344-28-1 Al2O3
PRO CQ 633293-93-3

RX(238) OF 354 COMPOSED OF RX(25), RX(33), RX(26), RX(27), RX(11)

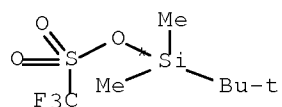
RX(238) CF + CI + L + CE + AV ==> AX



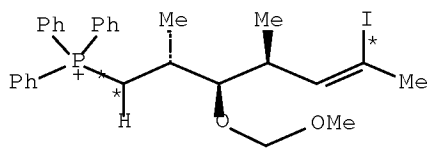
CF



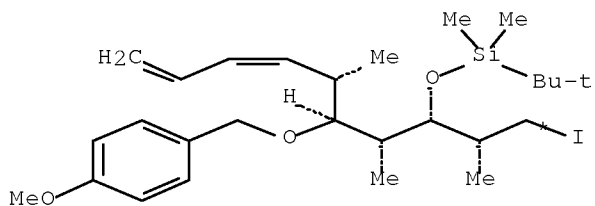
CI



L



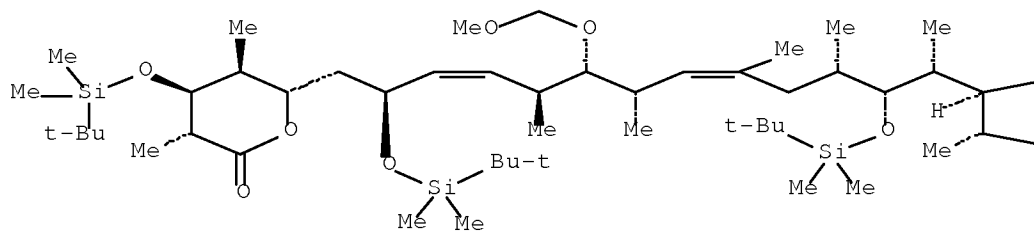
CE

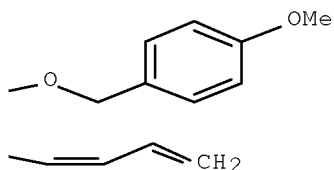


AV

5
STEPS
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AX
YIELD 50%

RX(25) RCT CF 252342-42-0

STAGE(1)

RGT CK 7550-45-0 TiCl4
SOL 75-09-2 CH2Cl2

STAGE(2)

RCT CI 130043-07-1
CON -78 deg C

STAGE(3)

RGT CL 76-05-1 F3CCO2H
SOL 110-54-3 Hexane
CON room temperature

PRO CJ 252342-43-1

RX(33) RCT CJ 252342-43-1

RGT CW 54575-49-4 K Selectride
PRO CM 256920-77-1
SOL 109-99-9 THF, 108-88-3 PhMe
NTE stereoselective, ratio of diastereomers = 9:1

RX(26) RCT CM 256920-77-1, L 69739-34-0

STAGE(1)

SOL 75-09-2 CH2Cl2

STAGE(2)

RGT AJ 10028-15-6 Ozone
SOL 75-09-2 CH2Cl2

STAGE(3)

RGT BE 603-35-0 PPh3

PRO CN 252342-51-1

NTE yield over 12 steps starting from Roche's ester = 33%

RX(27) RCT CE 850211-72-2, CN 252342-51-1

RGT CA 1070-89-9 (Me3Si)2N.Na
PRO AW 850211-74-4
CON -78 deg C -> -10 deg C
NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
 SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
 Pentane
 CON SUBSTAGE(1) room temperature -> -78 deg C
 SUBSTAGE(2) -78 deg C
 SUBSTAGE(3) -78 deg C -> room temperature
 SUBSTAGE(4) 1 hour, room temperature

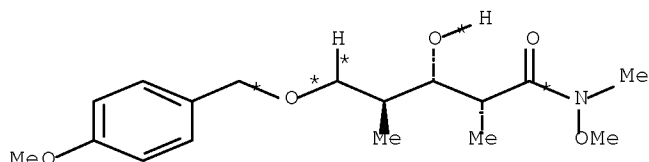
STAGE(2)

RCT AW 850211-74-4
 RGT BA 534-17-8 Cs2CO3
 CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

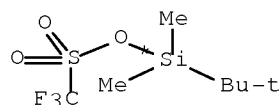
PRO AX 633293-75-1

NTE BBN related byproducts were obtained in 10% yield, Suzuki
 coupling

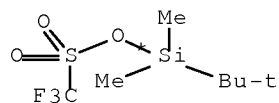
RX(239) OF 354 COMPOSED OF RX(24), RX(25), RX(33), RX(26), RX(27), RX(11)
 RX(239) BS + 2 L + CI + CE + AV ==> AX



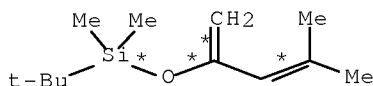
BS



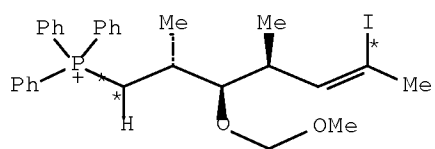
L



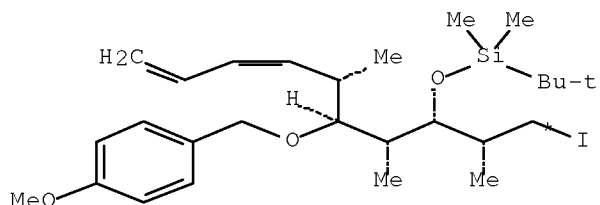
L



CI

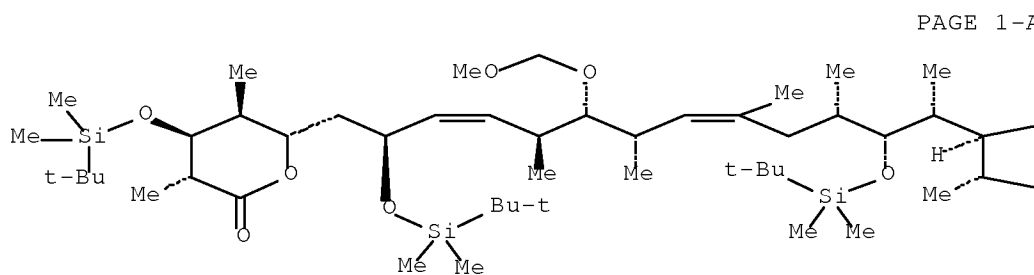


CE

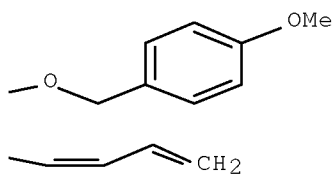


AV

6
STEPS
→



PAGE 1-A



AX
YIELD 50%

PAGE 1-B

RX(24) RCT BS 252342-49-7, L 69739-34-0

STAGE(1)

RGT N 108-48-5 2,6-Lutidine

STAGE(2)

RGT CG 1333-74-0 H2

CAT 12135-22-7 Pd(OH)₂
SOL 64-17-5 EtOH

STAGE(3)

RGT U 26412-87-3 Pyridine-SO₃ (1:1), E 7087-68-5 EtN(Pr-i)₂

PRO CF 252342-42-0

RX(25) RCT CF 252342-42-0

STAGE(1)

RGT CK 7550-45-0 TiCl₄
SOL 75-09-2 CH₂Cl₂

STAGE(2)

RCT CI 130043-07-1
CON -78 deg C

STAGE(3)

RGT CL 76-05-1 F₃CCO₂H
SOL 110-54-3 Hexane
CON room temperature

PRO CJ 252342-43-1

RX(33) RCT CJ 252342-43-1
RGT CW 54575-49-4 K Selectride
PRO CM 256920-77-1
SOL 109-99-9 THF, 108-88-3 PhMe
NTE stereoselective, ratio of diastereomers = 9:1

RX(26) RCT CM 256920-77-1, L 69739-34-0

STAGE(1)

SOL 75-09-2 CH₂Cl₂

STAGE(2)

RGT AJ 10028-15-6 Ozone
SOL 75-09-2 CH₂Cl₂

STAGE(3)

RGT BE 603-35-0 PPh₃

PRO CN 252342-51-1

NTE yield over 12 steps starting from Roche's ester = 33%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
RGT CA 1070-89-9 (Me₃Si)₂N.Na
PRO AW 850211-74-4
CON -78 deg C -> -10 deg C
NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
SOL 60-29-7 Et₂O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) -78 deg C

SUBSTAGE(3) -78 deg C -> room temperature
 SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AW 850211-74-4
 RGT BA 534-17-8 Cs2CO3
 CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

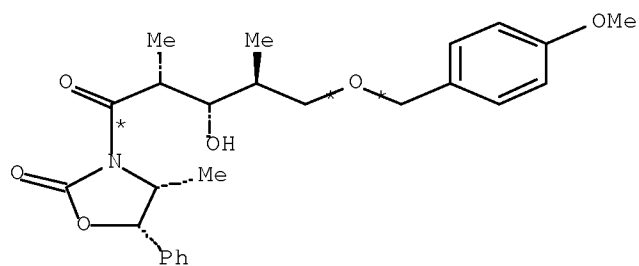
PRO AX 633293-75-1

NTE BBN related byproducts were obtained in 10% yield, Suzuki
 coupling

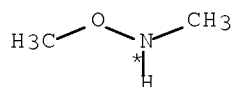
RX(240) OF 354 COMPOSED OF RX(17), RX(24), RX(25), RX(33), RX(26), RX(27),
 RX(11)

RX(240) BQ + BR + 2 L + CI + CE + AV ==>

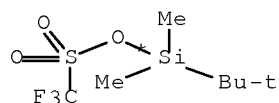
AX



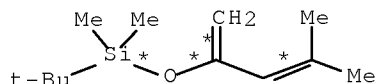
BQ



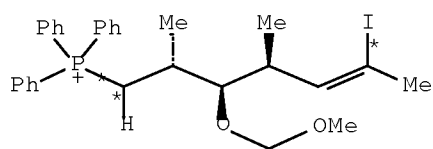
BR



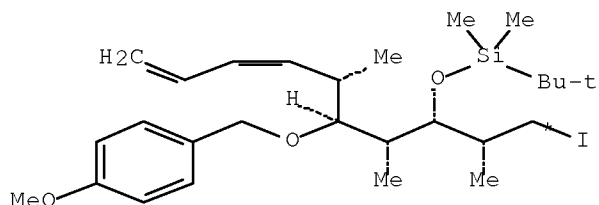
2 L



CI

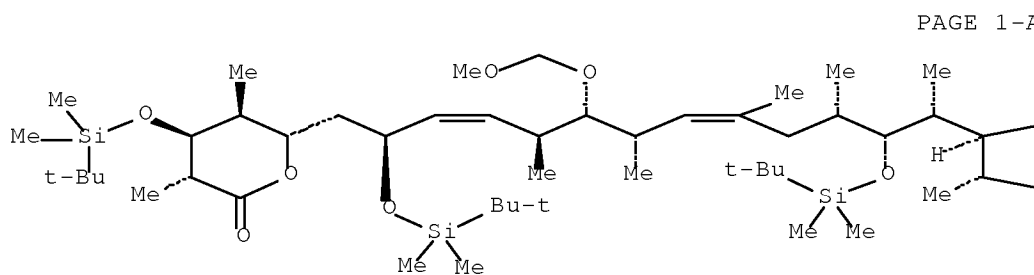


CE

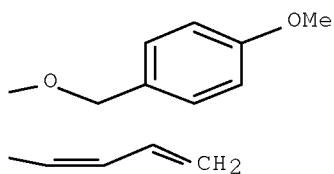


AV

7
STEPS
→



PAGE 1-A



AX
YIELD 50%

PAGE 1-B

RX(17) RCT BQ 132969-62-1, BR 6638-79-5
 RGT BT 75-24-1 AlMe3
 PRO BS 252342-49-7
 SOL 109-99-9 THF
 NTE yield over 5 steps starting from Roche's ester = 72%

RX(24) RCT BS 252342-49-7, L 69739-34-0

STAGE(1)
 RGT N 108-48-5 2,6-Lutidine

STAGE(2)
 RGT CG 1333-74-0 H2
 CAT 12135-22-7 Pd(OH)2
 SOL 64-17-5 EtOH

STAGE(3)
 RGT U 26412-87-3 Pyridine-SO3 (1:1), E 7087-68-5 EtN(Pr-i)2

PRO CF 252342-42-0

RX(25) RCT CF 252342-42-0

 STAGE(1)
 RGT CK 7550-45-0 TiCl4
 SOL 75-09-2 CH2Cl2

 STAGE(2)
 RCT CI 130043-07-1
 CON -78 deg C

 STAGE(3)
 RGT CL 76-05-1 F3CCO2H
 SOL 110-54-3 Hexane
 CON room temperature

PRO CJ 252342-43-1

RX(33) RCT CJ 252342-43-1
 RGT CW 54575-49-4 K Selectride
 PRO CM 256920-77-1
 SOL 109-99-9 THF, 108-88-3 PhMe
 NTE stereoselective, ratio of diastereomers = 9:1

RX(26) RCT CM 256920-77-1, L 69739-34-0

 STAGE(1)
 SOL 75-09-2 CH2Cl2

 STAGE(2)
 RGT AJ 10028-15-6 Ozone
 SOL 75-09-2 CH2Cl2

 STAGE(3)
 RGT BE 603-35-0 PPh3

PRO CN 252342-51-1
 NTE yield over 12 steps starting from Roche's ester = 33%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
 RGT CA 1070-89-9 (Me3Si)2N.Na
 PRO AW 850211-74-4
 CON -78 deg C -> -10 deg C
 NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
 SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
 Pentane
 CON SUBSTAGE(1) room temperature -> -78 deg C
 SUBSTAGE(2) -78 deg C
 SUBSTAGE(3) -78 deg C -> room temperature
 SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

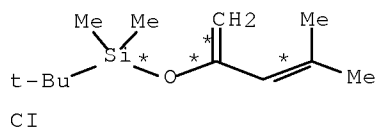
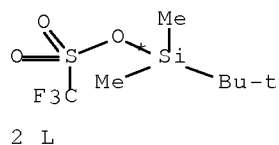
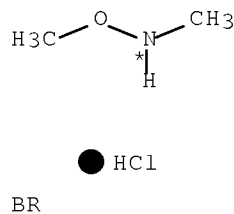
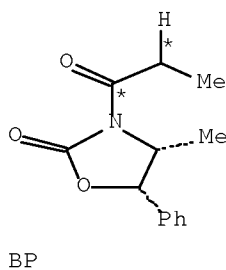
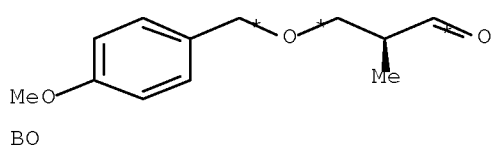
RCT AW 850211-74-4
 RGT BA 534-17-8 Cs2CO3
 CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

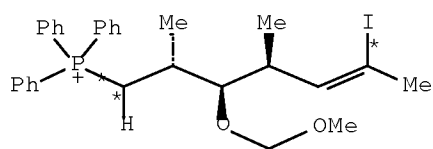
PRO AX 633293-75-1

NTE BBN related byproducts were obtained in 10% yield, Suzuki
 coupling

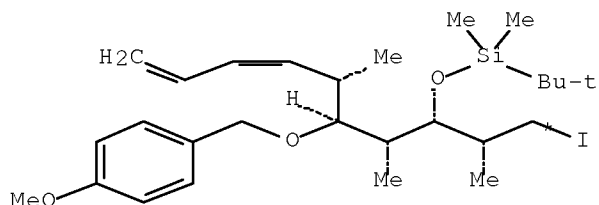
RX(241) OF 354 COMPOSED OF RX(16), RX(17), RX(24), RX(25), RX(33), RX(26),
 RX(27), RX(11)

RX(241) BO + BP + BR + 2 L + CI + CE + AV
 ==> AX



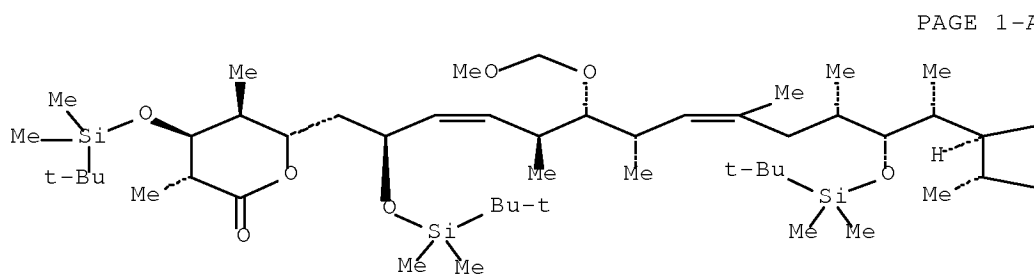


CE

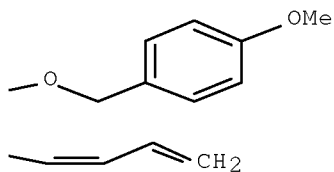


AV

8
STEPS
→



PAGE 1-A



PAGE 1-B

AX
YIELD 50%

RX(16) RCT BO 132969-60-9, BP 77877-20-4
RGT V 121-44-8 Et3N, F 60669-69-4 F3CSO3BBu2
PRO BQ 132969-62-1

RX(17) RCT BQ 132969-62-1, BR 6638-79-5
RGT BT 75-24-1 AlMe3
PRO BS 252342-49-7

SOL 109-99-9 THF
NTE yield over 5 steps starting from Roche's ester = 72%

RX(24) RCT BS 252342-49-7, L 69739-34-0

STAGE(1)
RGT N 108-48-5 2,6-Lutidine

STAGE(2)
RGT CG 1333-74-0 H2
CAT 12135-22-7 Pd(OH)2
SOL 64-17-5 EtOH

STAGE(3)
RGT U 26412-87-3 Pyridine-SO3 (1:1), E 7087-68-5 EtN(Pr-i)2

PRO CF 252342-42-0

RX(25) RCT CF 252342-42-0

STAGE(1)
RGT CK 7550-45-0 TiCl4
SOL 75-09-2 CH2Cl2

STAGE(2)
RCT CI 130043-07-1
CON -78 deg C

STAGE(3)
RGT CL 76-05-1 F3CCO2H
SOL 110-54-3 Hexane
CON room temperature

PRO CJ 252342-43-1

RX(33) RCT CJ 252342-43-1
RGT CW 54575-49-4 K Selectride
PRO CM 256920-77-1
SOL 109-99-9 THF, 108-88-3 PhMe
NTE stereoselective, ratio of diastereomers = 9:1

RX(26) RCT CM 256920-77-1, L 69739-34-0

STAGE(1)
SOL 75-09-2 CH2Cl2

STAGE(2)
RGT AJ 10028-15-6 Ozone
SOL 75-09-2 CH2Cl2

STAGE(3)
RGT BE 603-35-0 PPh3

PRO CN 252342-51-1
NTE yield over 12 steps starting from Roche's ester = 33%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
RGT CA 1070-89-9 (Me3Si)2N.Na
PRO AW 850211-74-4
CON -78 deg C -> -10 deg C

NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) -78 deg C
SUBSTAGE(3) -78 deg C -> room temperature
SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

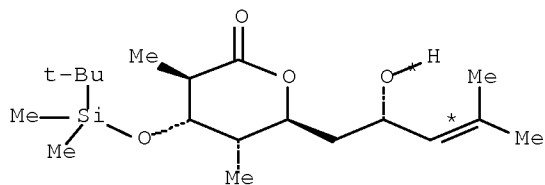
RCT AW 850211-74-4
RGT BA 534-17-8 Cs2CO3
CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

PRO AX 633293-75-1

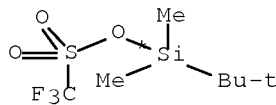
NTE BBN related byproducts were obtained in 10% yield, Suzuki
coupling

RX(242) OF 354 COMPOSED OF RX(26), RX(27), RX(11), RX(28), RX(29)

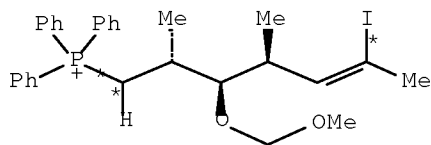
RX(242) CM + L + CE + AV + CP ==> CQ



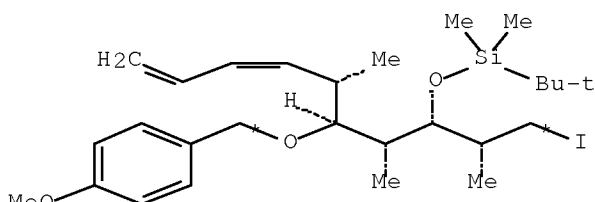
CM



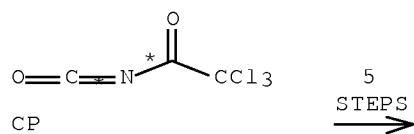
L



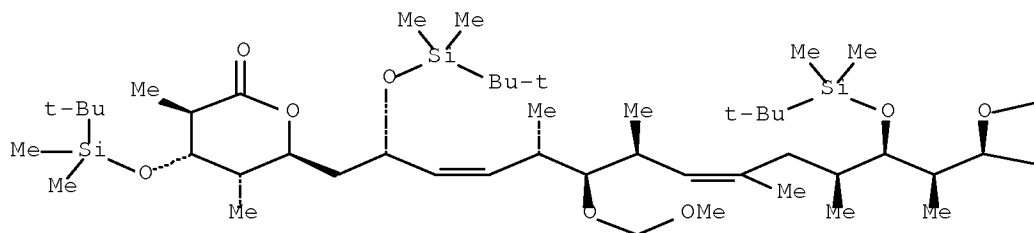
CE



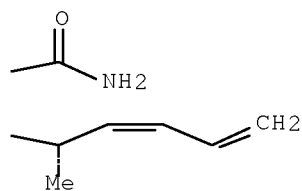
AV



PAGE 1-A



PAGE 1-B



CQ
 YIELD 92%

RX(26) RCT CM 256920-77-1, L 69739-34-0

STAGE(1)

SOL 75-09-2 CH₂Cl₂

STAGE(2)

RGT AJ 10028-15-6 Ozone

SOL 75-09-2 CH₂Cl₂

STAGE(3)

RGT BE 603-35-0 PPh₃

PRO CN 252342-51-1

NTE yield over 12 steps starting from Roche's ester = 33%

RX(27) RCT CE 850211-72-2, CN 252342-51-1

RGT CA 1070-89-9 (Me₃Si)₂N.Na

PRO AW 850211-74-4
 CON -78 deg C -> -10 deg C
 NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
 SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
 Pentane
 CON SUBSTAGE(1) room temperature -> -78 deg C
 SUBSTAGE(2) -78 deg C
 SUBSTAGE(3) -78 deg C -> room temperature
 SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AW 850211-74-4
 RGT BA 534-17-8 Cs2CO3
 CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

PRO AX 633293-75-1

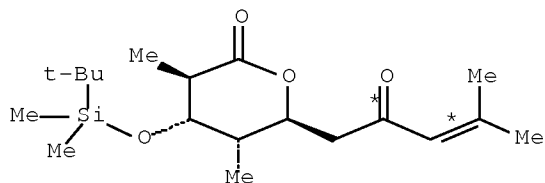
NTE BBN related byproducts were obtained in 10% yield, Suzuki
 coupling

RX(28) RCT AX 633293-75-1
 RGT CC 84-58-2 DDQ
 PRO CO 633293-76-2
 SOL 7732-18-5 Water, 75-09-2 CH2Cl2
 CON 0 - room temperature deg C

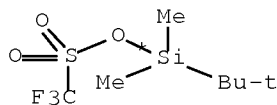
RX(29) RCT CO 633293-76-2, CP 3019-71-4
 RGT CR 1344-28-1 Al2O3
 PRO CQ 633293-93-3

RX(243) OF 354 COMPOSED OF RX(33), RX(26), RX(27), RX(11), RX(28), RX(29)

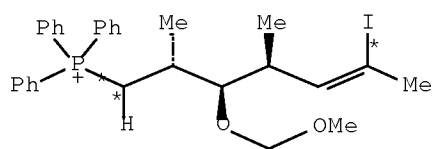
RX(243) CJ + L + CE + AV + CP ==> CQ



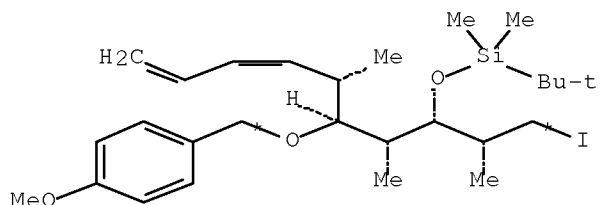
CJ



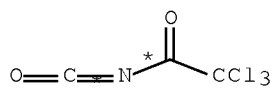
L



CE



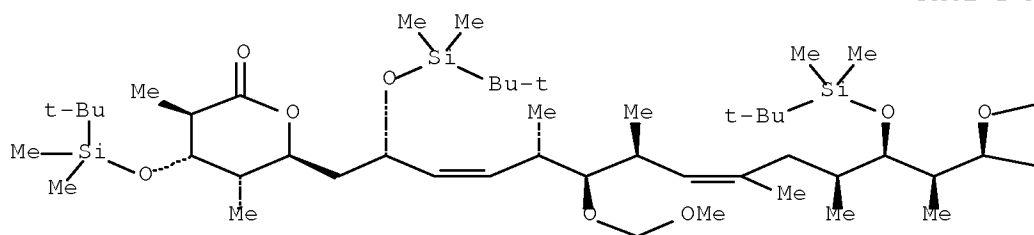
AV



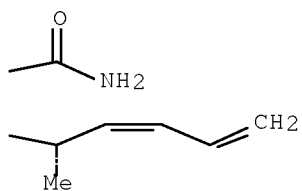
CP

6
STEPS
→

PAGE 1-A



PAGE 1-B



CO
YIELD 92%

RX(33) RCT CJ 252342-43-1
 RGT CW 54575-49-4 K Selectride
 PRO CM 256920-77-1

SOL 109-99-9 THF, 108-88-3 PhMe
NTE stereoselective, ratio of diastereomers = 9:1

RX(26) RCT CM 256920-77-1, L 69739-34-0

STAGE(1)
SOL 75-09-2 CH2Cl2

STAGE(2)
RGT AJ 10028-15-6 Ozone
SOL 75-09-2 CH2Cl2

STAGE(3)
RGT BE 603-35-0 PPh3

PRO CN 252342-51-1
NTE yield over 12 steps starting from Roche's ester = 33%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
RGT CA 1070-89-9 (Me3Si)2N.Na
PRO AW 850211-74-4
CON -78 deg C -> -10 deg C
NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)
RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0 Pentane
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) -78 deg C
SUBSTAGE(3) -78 deg C -> room temperature
SUBSTAGE(4) 1 hour, room temperature

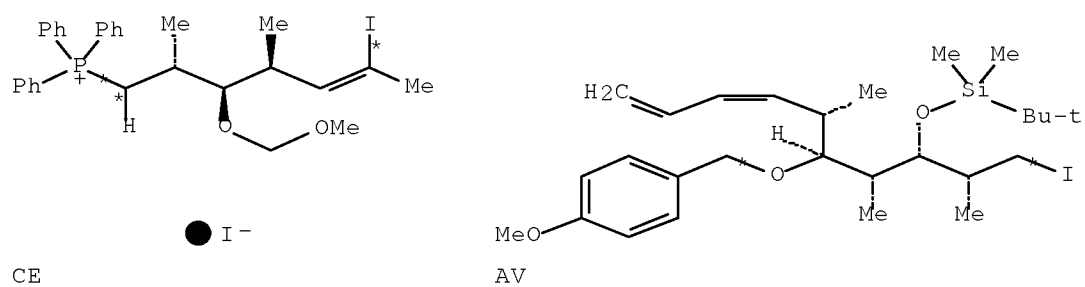
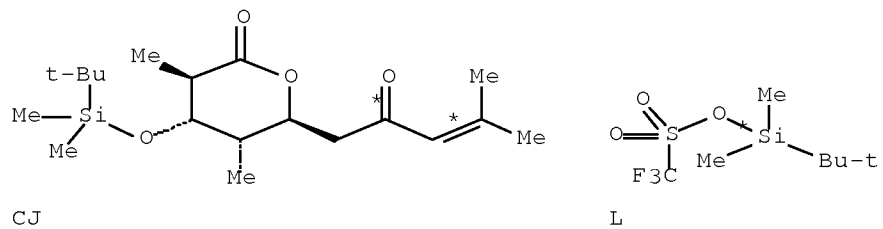
STAGE(2)
RCT AW 850211-74-4
RGT BA 534-17-8 Cs2CO3
CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

PRO AX 633293-75-1
NTE BBN related byproducts were obtained in 10% yield, Suzuki coupling

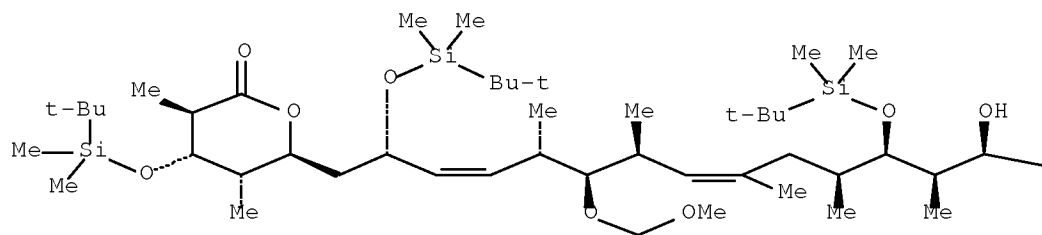
RX(28) RCT AX 633293-75-1
RGT CC 84-58-2 DDQ
PRO CO 633293-76-2
SOL 7732-18-5 Water, 75-09-2 CH2Cl2
CON 0 - room temperature deg C

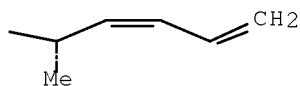
RX(29) RCT CO 633293-76-2, CP 3019-71-4
RGT CR 1344-28-1 Al2O3
PRO CQ 633293-93-3

RX(244) OF 354 COMPOSED OF RX(33), RX(26), RX(27), RX(11), RX(28)

$$\text{RX}(244) \quad \text{CJ} \quad + \quad \text{L} \quad + \quad \text{CE} \quad + \quad \text{AV} \quad ==> \quad \text{CO}$$


5
STEPS
→





CO
YIELD 91%

```

RX(33)    RCT  CJ 252342-43-1
          RGT  CW 54575-49-4 K Selectride
          PRO  CM 256920-77-1
          SOL  109-99-9 THF, 108-88-3 PhMe
          NTE  stereoselective, ratio of diastereomers = 9:1

RX(26)    RCT  CM 256920-77-1, L 69739-34-0

          STAGE(1)
            SOL  75-09-2 CH2Cl2

          STAGE(2)
            RGT  AJ 10028-15-6 Ozone
            SOL  75-09-2 CH2Cl2

          STAGE(3)
            RGT  BE 603-35-0 PPh3

          PRO  CN 252342-51-1
          NTE  yield over 12 steps starting from Roche's ester = 33%

RX(27)    RCT  CE 850211-72-2, CN 252342-51-1
          RGT  CA 1070-89-9 (Me3Si)2N.Na
          PRO  AW 850211-74-4
          CON  -78 deg C -> -10 deg C
          NTE  stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11)    RCT  AV 850211-69-7

          STAGE(1)
            RGT  AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
            SOL  60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
                  Pentane
            CON  SUBSTAGE(1) room temperature -> -78 deg C
                  SUBSTAGE(2) -78 deg C
                  SUBSTAGE(3) -78 deg C -> room temperature
                  SUBSTAGE(4) 1 hour, room temperature

          STAGE(2)
            RCT  AW 850211-74-4
            RGT  BA 534-17-8 Cs2CO3
            CAT  603-32-7 Ph3As, 72287-26-4 Palladium,
                  [1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
                  (SP-4-2)-

```

SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

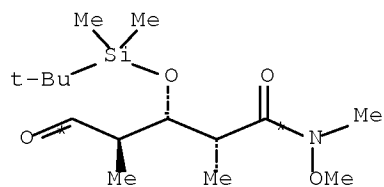
PRO AX 633293-75-1

NTE BBN related byproducts were obtained in 10% yield, Suzuki coupling

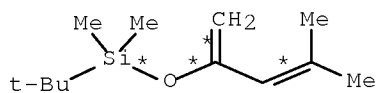
RX(28) RCT AX 633293-75-1
 RGT CC 84-58-2 DDQ
 PRO CO 633293-76-2
 SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
 CON 0 - room temperature deg C

RX(245) OF 354 COMPOSED OF RX(25), RX(33), RX(26), RX(27), RX(11), RX(28),
 RX(29)

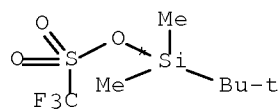
RX(245) CF + CI + L + CE + AV + CP ==>
 CQ



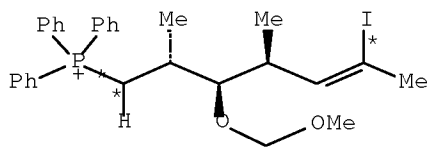
CF



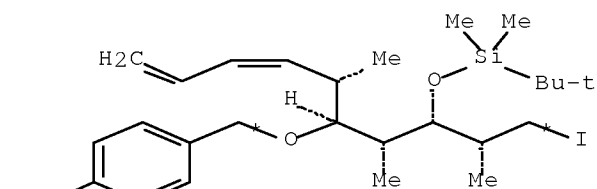
CI



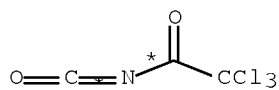
L



CE



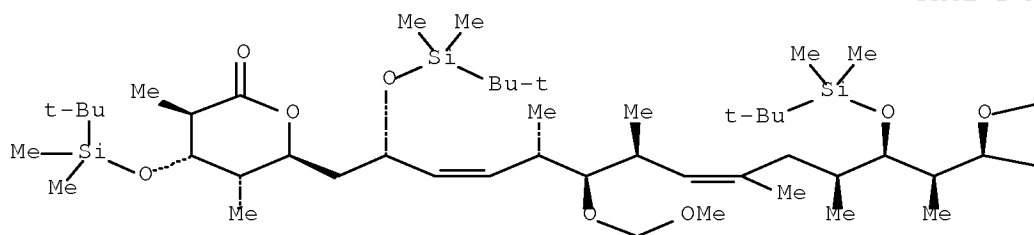
AV



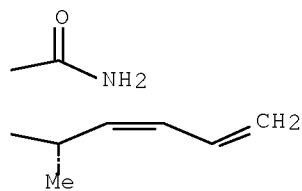
CP

7
STEPS
→

PAGE 1-A



PAGE 1-B



CO
YIELD 92%

RX(25) RCT CF 252342-42-0

STAGE(1)

RGT CK 7550-45-0 TiCl4

SOL 75-09-2 CH2Cl2

STAGE(2)

RCT CI 130043-07-1

CON -78 deg C

STAGE(3)

RGT CL 76-05-1 F3CCO2H

SOL 110-54-3 Hexane

CON room temperature

PRO CJ 252342-43-1

RX(33) RCT CJ 252342-43-1
 RGT CW 54575-49-4 K Selectride
 PRO CM 256920-77-1
 SOL 109-99-9 THF, 108-88-3 PhMe
 NTE stereoselective, ratio of diastereomers = 9:1

RX(26) RCT CM 256920-77-1, L 69739-34-0

 STAGE(1)
 SOL 75-09-2 CH2Cl2

 STAGE(2)
 RGT AJ 10028-15-6 Ozone
 SOL 75-09-2 CH2Cl2

 STAGE(3)
 RGT BE 603-35-0 PPh3

 PRO CN 252342-51-1
 NTE yield over 12 steps starting from Roche's ester = 33%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
 RGT CA 1070-89-9 (Me3Si)2N.Na
 PRO AW 850211-74-4
 CON -78 deg C -> -10 deg C
 NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

 STAGE(1)
 RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
 SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
 Pentane
 CON SUBSTAGE(1) room temperature -> -78 deg C
 SUBSTAGE(2) -78 deg C
 SUBSTAGE(3) -78 deg C -> room temperature
 SUBSTAGE(4) 1 hour, room temperature

 STAGE(2)
 RCT AW 850211-74-4
 RGT BA 534-17-8 Cs2CO3
 CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

 PRO AX 633293-75-1
 NTE BBN related byproducts were obtained in 10% yield, Suzuki
 coupling

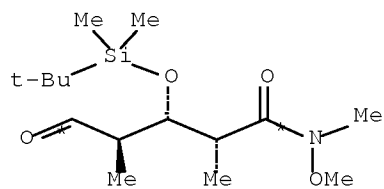
RX(28) RCT AX 633293-75-1
 RGT CC 84-58-2 DDQ
 PRO CO 633293-76-2
 SOL 7732-18-5 Water, 75-09-2 CH2Cl2
 CON 0 - room temperature deg C

RX(29) RCT CO 633293-76-2, CP 3019-71-4
 RGT CR 1344-28-1 Al2O3

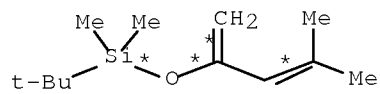
PRO CQ 633293--93--3

RX(246) OF 354 COMPOSED OF RX(25), RX(33), RX(26), RX(27), RX(11), RX(28)

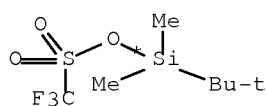
RX(246) CF + CI + L + CE + AV ==> CO



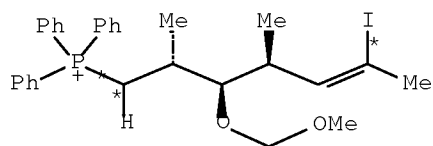
CF



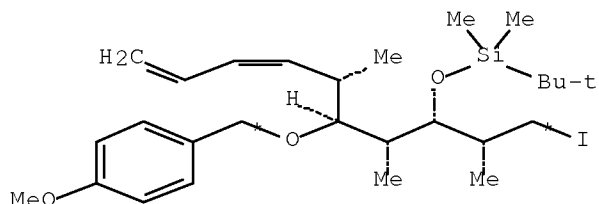
CI



L

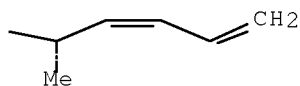
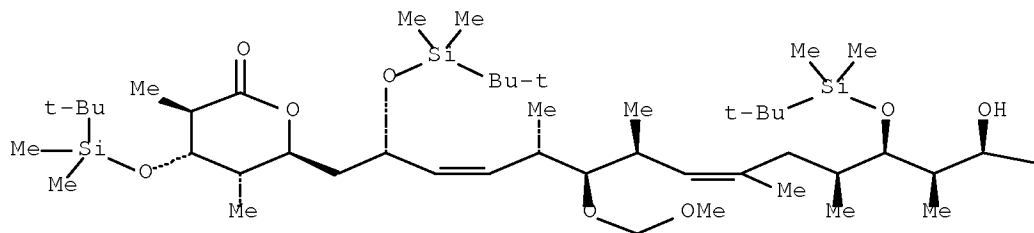


CE



AV

6
STEPS
→



CO
YIELD 91%

RX(25) RCT CF 252342-42-0

STAGE(1)

RGT CK 7550-45-0 TiCl₄

SOL 75-09-2 CH₂Cl₂

STAGE(2)

RCT CI 130043-07-1

CON -78 deg C

STAGE(3)

RGT CL 76-05-1 F₃CCO₂H

SOL 110-54-3 Hexane

CON room temperature

PRO CJ 252342-43-1

RX(33)

RCT CJ 252342-43-1

RGT CW 54575-49-4 K Selectride

PRO CM 256920-77-1

SOL 109-99-9 THF, 108-88-3 PhMe

NTE stereoselective, ratio of diastereomers = 9:1

RX(26)

RCT CM 256920-77-1, L 69739-34-0

STAGE(1)

SOL 75-09-2 CH₂Cl₂

STAGE(2)

RGT AJ 10028-15-6 Ozone
SOL 75-09-2 CH2Cl2

STAGE(3)

RGT BE 603-35-0 PPh3

PRO CN 252342-51-1

NTE yield over 12 steps starting from Roche's ester = 33%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
RGT CA 1070-89-9 (Me3Si)2N.Na
PRO AW 850211-74-4
CON -78 deg C -> -10 deg C
NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) -78 deg C
SUBSTAGE(3) -78 deg C -> room temperature
SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AW 850211-74-4
RGT BA 534-17-8 Cs2CO3
CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

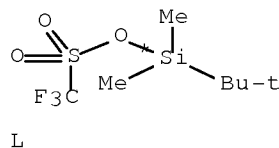
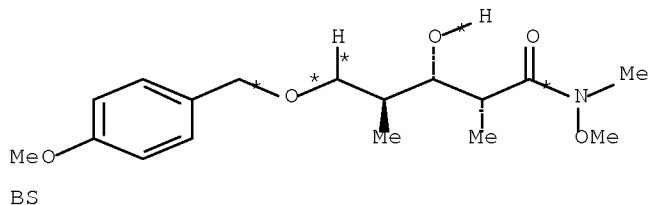
PRO AX 633293-75-1

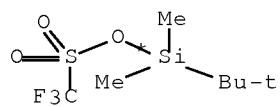
NTE BBN related byproducts were obtained in 10% yield, Suzuki
coupling

RX(28) RCT AX 633293-75-1
RGT CC 84-58-2 DDQ
PRO CO 633293-76-2
SOL 7732-18-5 Water, 75-09-2 CH2Cl2
CON 0 - room temperature deg C

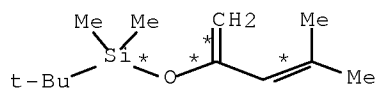
RX(247) OF 354 COMPOSED OF RX(24), RX(25), RX(33), RX(26), RX(27), RX(11),
RX(28), RX(29)

RX(247) BS + 2 L + CI + CE + AV + CP ==>
CQ

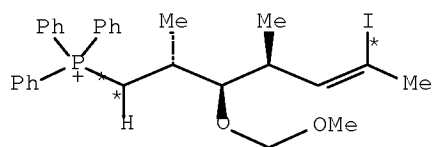




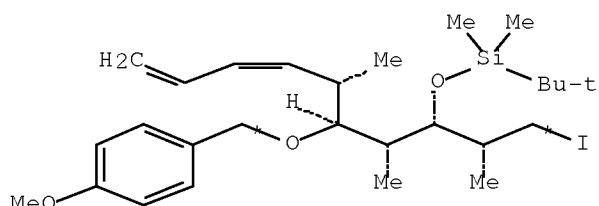
L



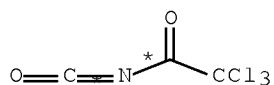
CI



CE



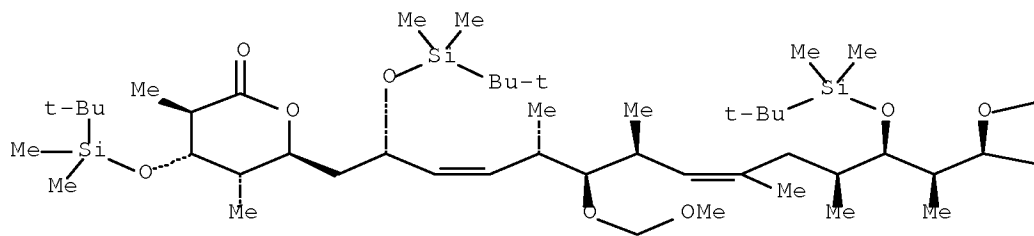
AV

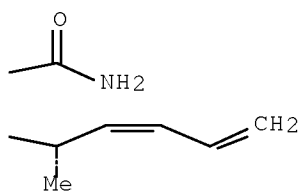


CP



PAGE 1-A





CO
YIELD 92%

RX(24) RCT BS 252342-49-7, L 69739-34-0

STAGE(1)

RGT N 108-48-5 2,6-Lutidine

STAGE(2)

RGT CG 1333-74-0 H2

CAT 12135-22-7 Pd(OH)2

SOL 64-17-5 EtOH

STAGE(3)

RGT U 26412-87-3 Pyridine-SO3 (1:1), E 7087-68-5 EtN(Pr-i)2

PRO CF 252342-42-0

RX(25) RCT CF 252342-42-0

STAGE(1)

RGT CK 7550-45-0 TiCl4

SOL 75-09-2 CH2Cl2

STAGE(2)

RCT CI 130043-07-1

CON -78 deg C

STAGE(3)

RGT CL 76-05-1 F3CCO2H

SOL 110-54-3 Hexane

CON room temperature

PRO CJ 252342-43-1

RX(33) RCT CJ 252342-43-1

RGT CW 54575-49-4 K Selectride

PRO CM 256920-77-1

SOL 109-99-9 THF, 108-88-3 PhMe

NTE stereoselective, ratio of diastereomers = 9:1

RX(26) RCT CM 256920-77-1, L 69739-34-0

STAGE(1)

SOL 75-09-2 CH2Cl2

STAGE(2)

RGT AJ 10028-15-6 Ozone
SOL 75-09-2 CH2Cl2

STAGE(3)

RGT BE 603-35-0 PPh3

PRO CN 252342-51-1

NTE yield over 12 steps starting from Roche's ester = 33%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
RGT CA 1070-89-9 (Me3Si)2N.Na
PRO AW 850211-74-4
CON -78 deg C -> -10 deg C
NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi

SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane

CON SUBSTAGE(1) room temperature -> -78 deg C

SUBSTAGE(2) -78 deg C

SUBSTAGE(3) -78 deg C -> room temperature

SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AW 850211-74-4

RGT BA 534-17-8 Cs2CO3

CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-

SOL 7732-18-5 Water, 68-12-2 DMF

CON 20 hours, room temperature

PRO AX 633293-75-1

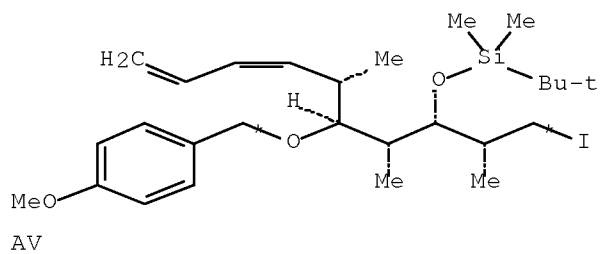
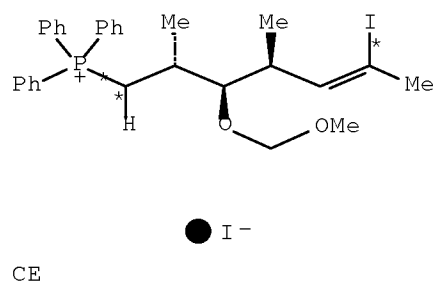
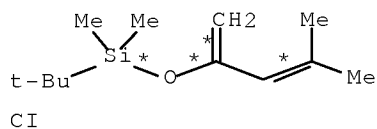
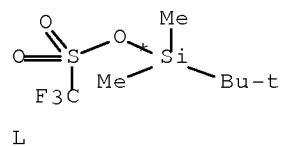
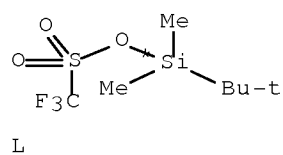
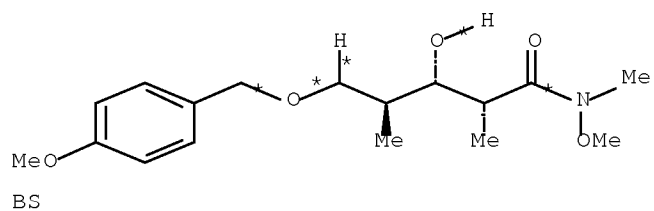
NTE BBN related byproducts were obtained in 10% yield, Suzuki
coupling

RX(28) RCT AX 633293-75-1
RGT CC 84-58-2 DDQ
PRO CO 633293-76-2
SOL 7732-18-5 Water, 75-09-2 CH2Cl2
CON 0 - room temperature deg C

RX(29) RCT CO 633293-76-2, CP 3019-71-4
RGT CR 1344-28-1 Al2O3
PRO CQ 633293-93-3

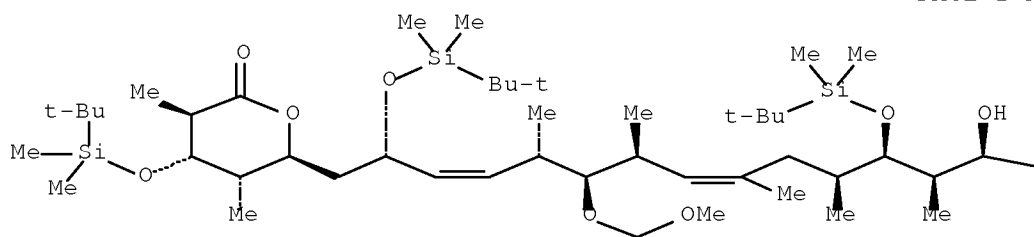
RX(248) OF 354 COMPOSED OF RX(24), RX(25), RX(33), RX(26), RX(27), RX(11),
RX(28)

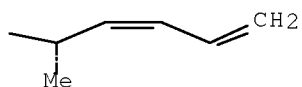
RX(248) BS + 2 L + CI + CE + AV ==> CO



7
 STEPS

PAGE 1-A





CO
YIELD 91%

RX(24) RCT BS 252342-49-7, L 69739-34-0

STAGE(1)

RGT N 108-48-5 2,6-Lutidine

STAGE(2)

RGT CG 1333-74-0 H₂

CAT 12135-22-7 Pd(OH)₂

SOL 64-17-5 EtOH

STAGE(3)

RGT U 26412-87-3 Pyridine-SO₃ (1:1), E 7087-68-5 EtN(Pr-i)₂

PRO CF 252342-42-0

RX(25) RCT CF 252342-42-0

STAGE(1)

RGT CK 7550-45-0 TiCl₄

SOL 75-09-2 CH₂Cl₂

STAGE(2)

RCT CI 130043-07-1

CON -78 deg C

STAGE(3)

RGT CL 76-05-1 F₃CCO₂H

SOL 110-54-3 Hexane

CON room temperature

PRO CJ 252342-43-1

RX(33) RCT CJ 252342-43-1

RGT CW 54575-49-4 K Selectride

PRO CM 256920-77-1

SOL 109-99-9 THF, 108-88-3 PhMe

NTE stereoselective, ratio of diastereomers = 9:1

RX(26) RCT CM 256920-77-1, L 69739-34-0

STAGE(1)

SOL 75-09-2 CH2Cl2

STAGE(2)

RGT AJ 10028-15-6 Ozone

SOL 75-09-2 CH2Cl2

STAGE(3)

RGT BE 603-35-0 PPh3

PRO CN 252342-51-1

NTE yield over 12 steps starting from Roche's ester = 33%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
RGT CA 1070-89-9 (Me3Si)2N.Na
PRO AW 850211-74-4
CON -78 deg C -> -10 deg C
NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi

SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane

CON SUBSTAGE(1) room temperature -> -78 deg C

SUBSTAGE(2) -78 deg C

SUBSTAGE(3) -78 deg C -> room temperature

SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AW 850211-74-4

RGT BA 534-17-8 Cs2CO3

CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-

SOL 7732-18-5 Water, 68-12-2 DMF

CON 20 hours, room temperature

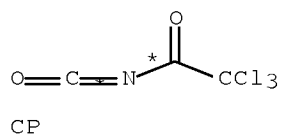
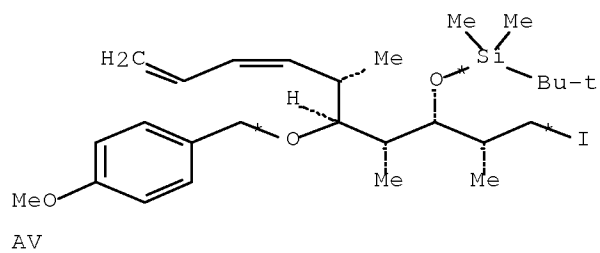
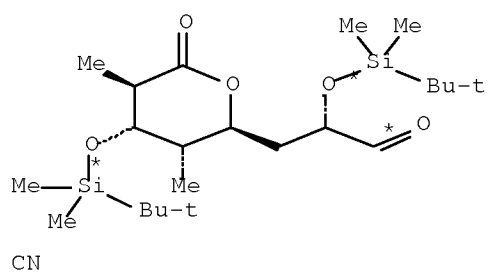
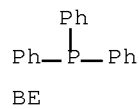
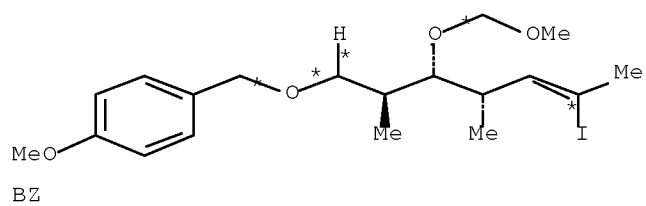
PRO AX 633293-75-1

NTE BBN related byproducts were obtained in 10% yield, Suzuki
coupling

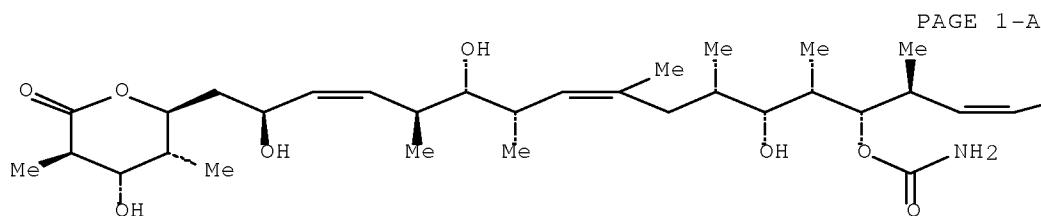
RX(28) RCT AX 633293-75-1
RGT CC 84-58-2 DDQ
PRO CO 633293-76-2
SOL 7732-18-5 Water, 75-09-2 CH2Cl2
CON 0 - room temperature deg C

RX(249) OF 354 COMPOSED OF RX(21), RX(22), RX(23), RX(27), RX(11), RX(28),
RX(29), RX(30)

RX(249) BZ + BE + CN + AV + CP ==> CS



8
 STEPS





CS
YIELD 95%

RX(21) RCT BZ 633294-02-7
RGT CC 84-58-2 DDQ
PRO CB 850211-70-0
SOL 7732-18-5 Water

RX(22) RCT CB 850211-70-0
RGT BE 603-35-0 PPh3, BF 7553-56-2 I2, BG 288-32-4 1H-Imidazole
PRO CD 850211-71-1

RX(23) RCT CD 850211-71-1, BE 603-35-0
PRO CE 850211-72-2
CON 100 deg C
NTE yield over 11 steps starting from Roche's ester = 27%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
RGT CA 1070-89-9 (Me3Si)2N.Na
PRO AW 850211-74-4
CON -78 deg C -> -10 deg C
NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0 Pentane
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) -78 deg C
SUBSTAGE(3) -78 deg C -> room temperature
SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AW 850211-74-4
RGT BA 534-17-8 Cs2CO3
CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

PRO AX 633293-75-1
NTE BBN related byproducts were obtained in 10% yield, Suzuki coupling

RX(28) RCT AX 633293-75-1

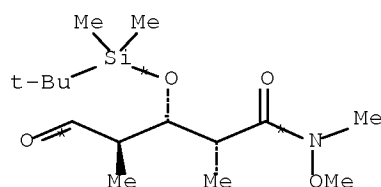
RGT CC 84-58-2 DDQ
 PRO CO 633293-76-2
 SOL 7732-18-5 Water, 75-09-2 CH2Cl2
 CON 0 - room temperature deg C

RX(29) RCT CO 633293-76-2, CP 3019-71-4
 RGT CR 1344-28-1 Al2O3
 PRO CQ 633293-93-3

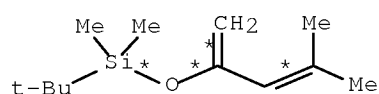
RX(30) RCT CQ 633293-93-3
 RGT CT 7647-01-0 HCl
 PRO CS 127943-53-7
 SOL 7732-18-5 Water, 67-56-1 MeOH
 NTE overall yield via iodine substituted pyran-2-one intermediate = 10%

RX(250) OF 354 COMPOSED OF RX(25), RX(33), RX(26), RX(27), RX(11), RX(28),
 RX(29), RX(30)

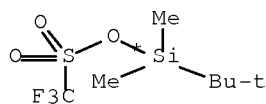
RX(250) CF + CI + L + CE + AV + CP ==>
 CS



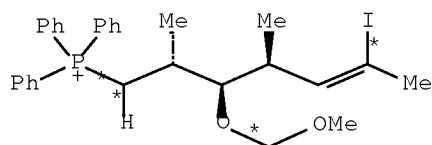
CF



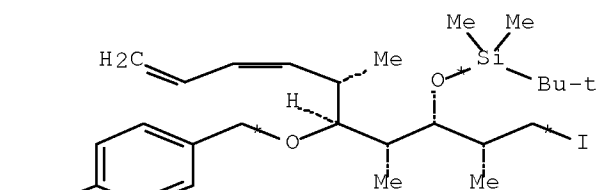
CI



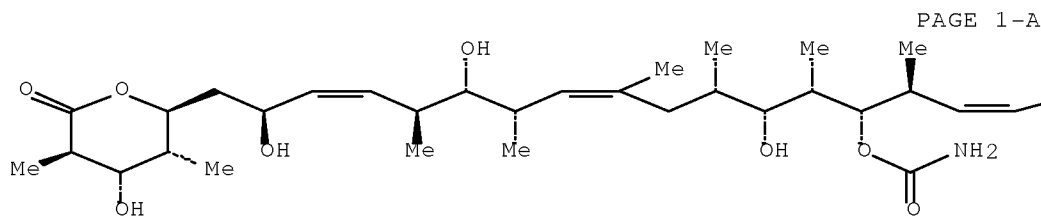
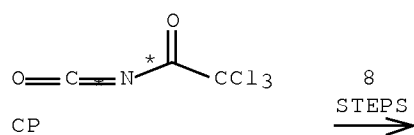
L



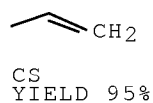
CE



AV



PAGE 1-B



RX(25) RCT CF 252342-42-0

STAGE(1)

RGT CK 7550-45-0 TiCl₄

SOL 75-09-2 CH₂Cl₂

STAGE(2)

RCT CI 130043-07-1

CON -78 deg C

STAGE(3)

RGT CL 76-05-1 F₃CCO₂H

SOL 110-54-3 Hexane

CON room temperature

PRO CJ 252342-43-1

RX(33)

RCT CJ 252342-43-1

RGT CW 54575-49-4 K Selectride

PRO CM 256920-77-1

SOL 109-99-9 THF, 108-88-3 PhMe

NTE stereoselective, ratio of diastereomers = 9:1

RX(26) RCT CM 256920-77-1, L 69739-34-0

STAGE(1)
SOL 75-09-2 CH2Cl2

STAGE(2)
RGT AJ 10028-15-6 Ozone
SOL 75-09-2 CH2Cl2

STAGE(3)
RGT BE 603-35-0 PPh3

PRO CN 252342-51-1
NTE yield over 12 steps starting from Roche's ester = 33%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
RGT CA 1070-89-9 (Me3Si)2N.Na
PRO AW 850211-74-4
CON -78 deg C -> -10 deg C
NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)
RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0 Pentane
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) -78 deg C
SUBSTAGE(3) -78 deg C -> room temperature
SUBSTAGE(4) 1 hour, room temperature

STAGE(2)
RCT AW 850211-74-4
RGT BA 534-17-8 Cs2CO3
CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

PRO AX 633293-75-1
NTE BBN related byproducts were obtained in 10% yield, Suzuki coupling

RX(28) RCT AX 633293-75-1
RGT CC 84-58-2 DDQ
PRO CO 633293-76-2
SOL 7732-18-5 Water, 75-09-2 CH2Cl2
CON 0 - room temperature deg C

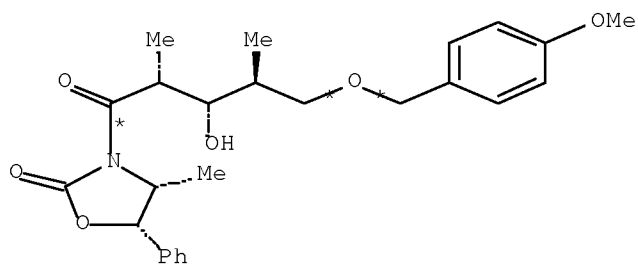
RX(29) RCT CO 633293-76-2, CP 3019-71-4
RGT CR 1344-28-1 Al2O3
PRO CQ 633293-93-3

RX(30) RCT CQ 633293-93-3
RGT CT 7647-01-0 HCl
PRO CS 127943-53-7
SOL 7732-18-5 Water, 67-56-1 MeOH
NTE overall yield via iodine substituted pyran-2-one intermediate =

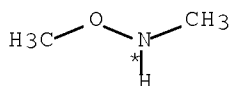
10%

RX(252) OF 354 COMPOSED OF RX(17), RX(24), RX(25), RX(33), RX(26), RX(27),
RX(11), RX(28)

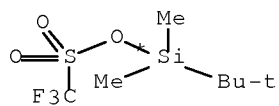
RX(252) BQ + BR + 2 L + CI + CE + AV ==>
CO



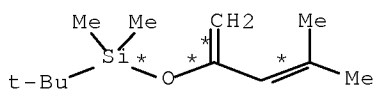
BQ



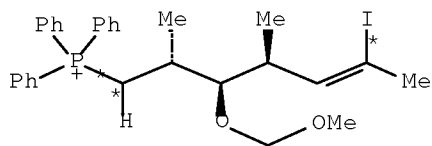
BR



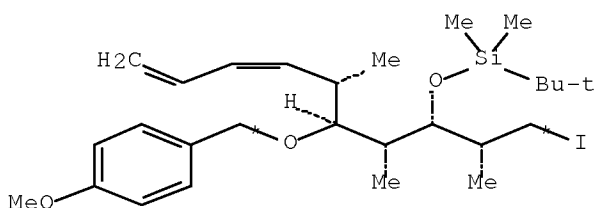
2 L



CI

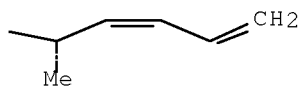
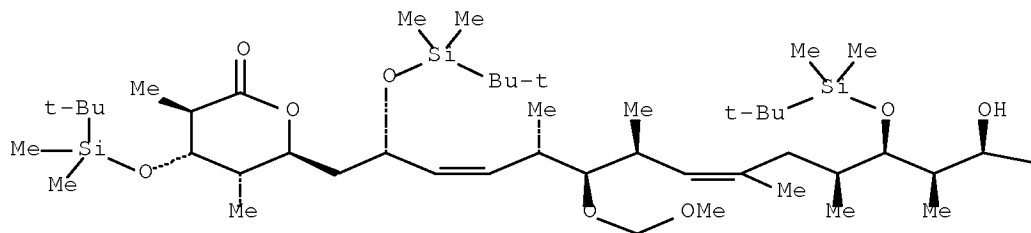


CE



AV

8
STEPS
→



CO
YIELD 91%

RX(17) RCT BQ 132969-62-1, BR 6638-79-5
 RGT BT 75-24-1 AlMe₃
 PRO BS 252342-49-7
 SOL 109-99-9 THF
 NTE yield over 5 steps starting from Roche's ester = 72%

RX(24) RCT BS 252342-49-7, L 69739-34-0

STAGE(1)
 RGT N 108-48-5 2,6-Lutidine

STAGE(2)
 RGT CG 1333-74-0 H₂
 CAT 12135-22-7 Pd(OH)₂
 SOL 64-17-5 EtOH

STAGE(3)
 RGT U 26412-87-3 Pyridine-SO₃ (1:1), E 7087-68-5 EtN(Pr-i)₂

PRO CF 252342-42-0

RX(25) RCT CF 252342-42-0

STAGE(1)
 RGT CK 7550-45-0 TiCl₄
 SOL 75-09-2 CH₂Cl₂

STAGE(2)
 RCT CI 130043-07-1

CON -78 deg C

STAGE(3)

RGT CL 76-05-1 F3CCO2H
SOL 110-54-3 Hexane
CON room temperature

PRO CJ 252342-43-1

RX(33) RCT CJ 252342-43-1
RGT CW 54575-49-4 K Selectride
PRO CM 256920-77-1
SOL 109-99-9 THF, 108-88-3 PhMe
NTE stereoselective, ratio of diastereomers = 9:1

RX(26) RCT CM 256920-77-1, L 69739-34-0

STAGE(1)

SOL 75-09-2 CH2Cl2

STAGE(2)

RGT AJ 10028-15-6 Ozone
SOL 75-09-2 CH2Cl2

STAGE(3)

RGT BE 603-35-0 PPh3

PRO CN 252342-51-1

NTE yield over 12 steps starting from Roche's ester = 33%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
RGT CA 1070-89-9 (Me3Si)2N.Na
PRO AW 850211-74-4
CON -78 deg C -> -10 deg C
NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) -78 deg C
SUBSTAGE(3) -78 deg C -> room temperature
SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AW 850211-74-4
RGT BA 534-17-8 Cs2CO3
CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

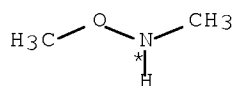
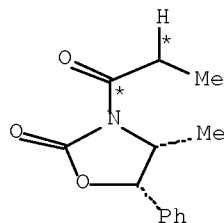
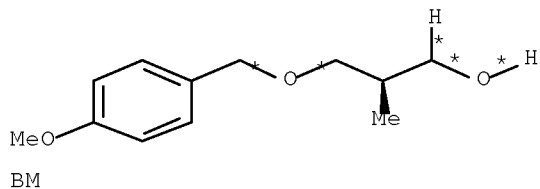
PRO AX 633293-75-1

NTE BBN related byproducts were obtained in 10% yield, Suzuki
coupling

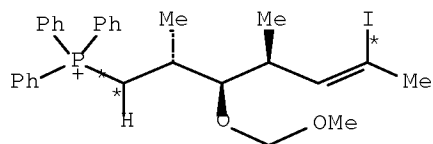
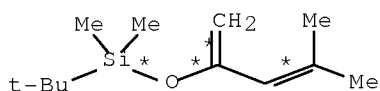
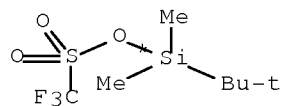
RX(28) RCT AX 633293-75-1
 RGT CC 84-58-2 DDQ
 PRO CO 633293-76-2
 SOL 7732-18-5 Water, 75-09-2 CH2Cl2
 CON 0 - room temperature deg C

RX(304) OF 354 COMPOSED OF RX(15), RX(16), RX(17), RX(24), RX(25), RX(33),
 RX(26), RX(27), RX(11)

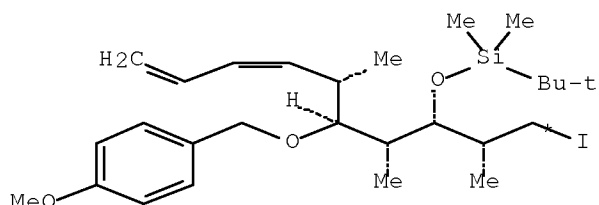
RX(304) BM + BP + BR + 2 L + CI + CE + AV
 ==> AX



● HCl

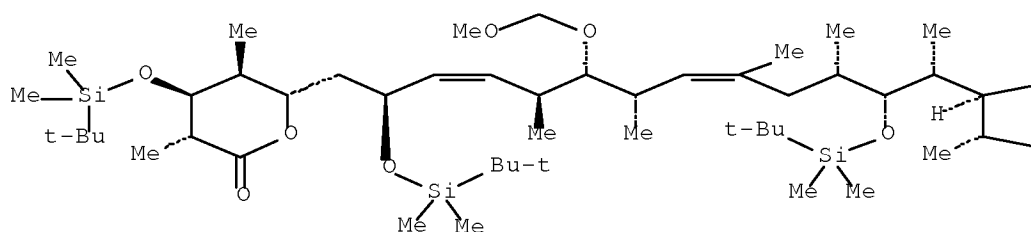


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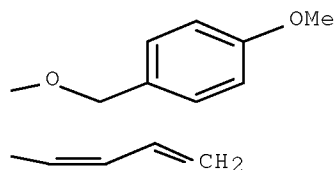


9
STEPS
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PAGE 1-A



PAGE 1-B



AX
YIELD 50%

RX(15)	RCT	BM 136320-64-4
	PRO	BO 132969-60-9
	NTE	Swern oxidation
RX(16)	RCT	BO 132969-60-9, BP 77877-20-4
	RGT	V 121-44-8 Et3N, F 60669-69-4 F3CSO3BBu2
	PRO	BQ 132969-62-1
RX(17)	RCT	BQ 132969-62-1, BR 6638-79-5
	RGT	BT 75-24-1 AlMe3
	PRO	BS 252342-49-7
	SOL	109-99-9 THF
	NTE	yield over 5 steps starting from Roche's ester = 72%
RX(24)	RCT	BS 252342-49-7, L 69739-34-0
	STAGE(1)	
	RGT	N 108-48-5 2,6-Lutidine
	STAGE(2)	
	RGT	CG 1333-74-0 H2

CAT 12135-22-7 Pd(OH)₂
SOL 64-17-5 EtOH

STAGE(3)

RGT U 26412-87-3 Pyridine-SO₃ (1:1), E 7087-68-5 EtN(Pr-i)₂

PRO CF 252342-42-0

RX(25) RCT CF 252342-42-0

STAGE(1)

RGT CK 7550-45-0 TiCl₄
SOL 75-09-2 CH₂Cl₂

STAGE(2)

RCT CI 130043-07-1
CON -78 deg C

STAGE(3)

RGT CL 76-05-1 F₃CCO₂H
SOL 110-54-3 Hexane
CON room temperature

PRO CJ 252342-43-1

RX(33) RCT CJ 252342-43-1
RGT CW 54575-49-4 K Selectride
PRO CM 256920-77-1
SOL 109-99-9 THF, 108-88-3 PhMe
NTE stereoselective, ratio of diastereomers = 9:1

RX(26) RCT CM 256920-77-1, L 69739-34-0

STAGE(1)

SOL 75-09-2 CH₂Cl₂

STAGE(2)

RGT AJ 10028-15-6 Ozone
SOL 75-09-2 CH₂Cl₂

STAGE(3)

RGT BE 603-35-0 PPh₃

PRO CN 252342-51-1

NTE yield over 12 steps starting from Roche's ester = 33%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
RGT CA 1070-89-9 (Me₃Si)₂N.Na
PRO AW 850211-74-4
CON -78 deg C -> -10 deg C
NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
SOL 60-29-7 Et₂O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) -78 deg C

SUBSTAGE(3) -78 deg C -> room temperature
 SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

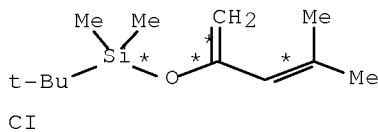
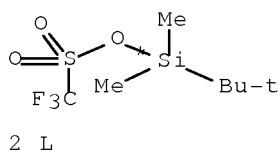
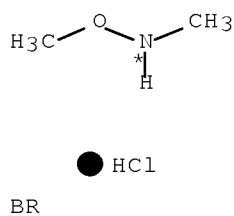
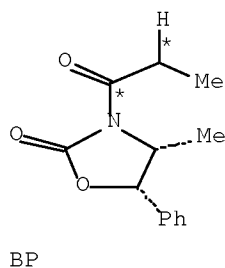
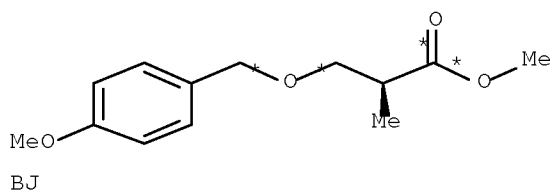
RCT AW 850211-74-4
 RGT BA 534-17-8 Cs2CO3
 CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

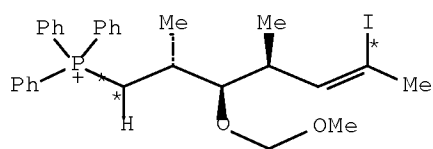
PRO AX 633293-75-1

NTE BBN related byproducts were obtained in 10% yield, Suzuki
 coupling

RX(306) OF 354 COMPOSED OF RX(14), RX(15), RX(16), RX(17), RX(24), RX(25),
 RX(33), RX(26), RX(27), RX(11)

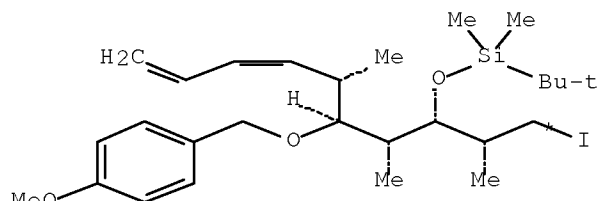
RX(306) BJ + BP + BR + 2 L + CI + CE + AV
 ==> AX





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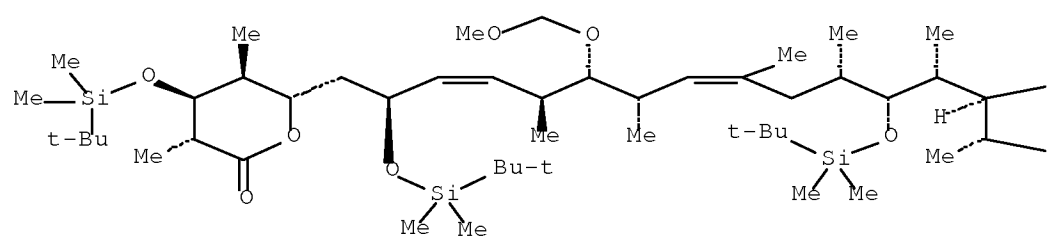
CE



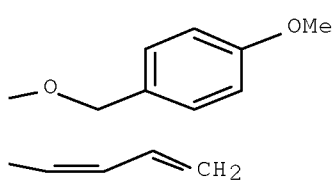
AV

10
STEPS
→

PAGE 1-A



PAGE 1-B



AX
YIELD 50%

RX(14)	RCT	BJ	132969-71-2
	RGT	BN	16853-85-3 LiAlH ₄
	PRO	BM	136320-64-4
	SOL	109-99-9	THF
RX(15)	RCT	BM	136320-64-4
	PRO	BO	132969-60-9

NTE Swern oxidation

RX(16) RCT BO 132969-60-9, BP 77877-20-4
RGT V 121-44-8 Et3N, F 60669-69-4 F3CSO3BBu2
PRO BQ 132969-62-1

RX(17) RCT BQ 132969-62-1, BR 6638-79-5
RGT BT 75-24-1 AlMe3
PRO BS 252342-49-7
SOL 109-99-9 THF
NTE yield over 5 steps starting from Roche's ester = 72%

RX(24) RCT BS 252342-49-7, L 69739-34-0

STAGE(1)
RGT N 108-48-5 2,6-Lutidine

STAGE(2)
RGT CG 1333-74-0 H2
CAT 12135-22-7 Pd(OH)2
SOL 64-17-5 EtOH

STAGE(3)
RGT U 26412-87-3 Pyridine-SO3 (1:1), E 7087-68-5 EtN(Pr-i)2

PRO CF 252342-42-0

RX(25) RCT CF 252342-42-0

STAGE(1)
RGT CK 7550-45-0 TiCl4
SOL 75-09-2 CH2Cl2

STAGE(2)
RCT CI 130043-07-1
CON -78 deg C

STAGE(3)
RGT CL 76-05-1 F3CCO2H
SOL 110-54-3 Hexane
CON room temperature

PRO CJ 252342-43-1

RX(33) RCT CJ 252342-43-1
RGT CW 54575-49-4 K Selectride
PRO CM 256920-77-1
SOL 109-99-9 THF, 108-88-3 PhMe
NTE stereoselective, ratio of diastereomers = 9:1

RX(26) RCT CM 256920-77-1, L 69739-34-0

STAGE(1)
SOL 75-09-2 CH2Cl2

STAGE(2)
RGT AJ 10028-15-6 Ozone
SOL 75-09-2 CH2Cl2

STAGE(3)

RGT BE 603-35-0 PPh3

PRO CN 252342-51-1

NTE yield over 12 steps starting from Roche's ester = 33%

RX(27) RCT CE 850211-72-2, CN 252342-51-1

RGT CA 1070-89-9 (Me3Si)2N.Na

PRO AW 850211-74-4

CON -78 deg C -> -10 deg C

NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi

SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0 Pentane

CON SUBSTAGE(1) room temperature -> -78 deg C

SUBSTAGE(2) -78 deg C

SUBSTAGE(3) -78 deg C -> room temperature

SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AW 850211-74-4

RGT BA 534-17-8 Cs2CO3

CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-

SOL 7732-18-5 Water, 68-12-2 DMF

CON 20 hours, room temperature

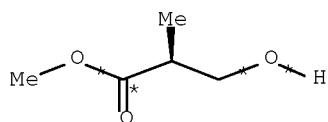
PRO AX 633293-75-1

NTE BBN related byproducts were obtained in 10% yield, Suzuki coupling

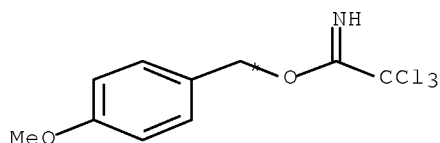
RX(308) OF 354 COMPOSED OF RX(13), RX(14), RX(15), RX(16), RX(17), RX(24),
RX(25), RX(33), RX(26), RX(27), RX(11)

RX(308) BI + AD + BP + BR + 2 L + CI + CE +

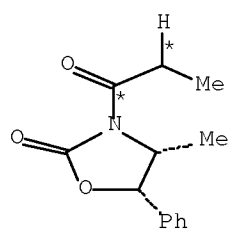
AV ==> AX



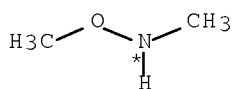
BI



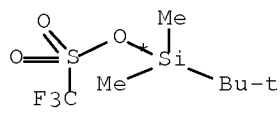
AD



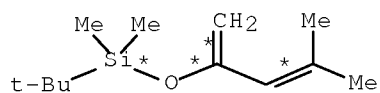
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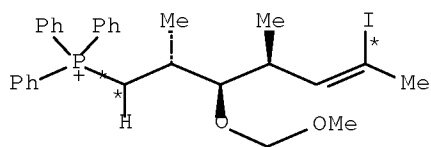
BR



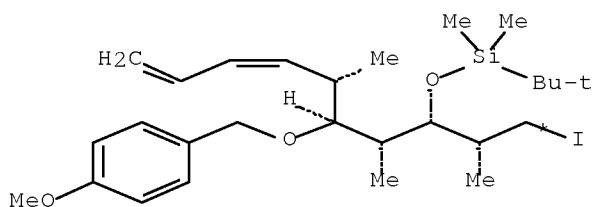
2 L



CI



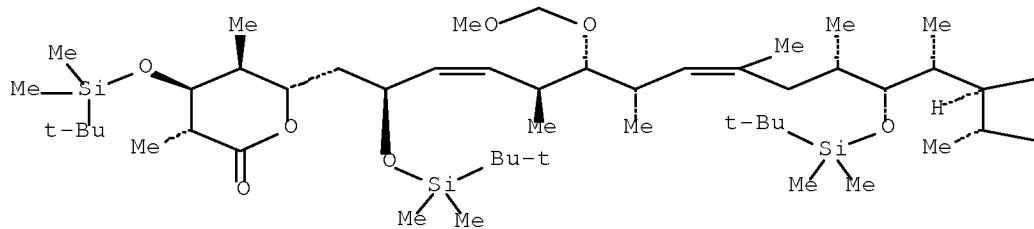
CE

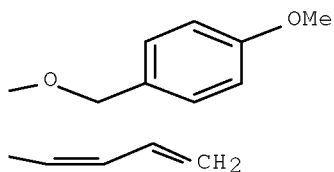


AV

11
STEPS
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PAGE 1-A





AX
YIELD 50%

RX(13) RCT BI 80657-57-4, AD 89238-99-3
RGT BK 24057-28-1 Pyridinium tosylate
PRO BJ 132969-71-2
SOL 75-09-2 CH2Cl2, 110-82-7 Cyclohexane

RX(14) RCT BJ 132969-71-2
RGT BN 16853-85-3 LiAlH4
PRO BM 136320-64-4
SOL 109-99-9 THF

RX(15) RCT BM 136320-64-4
PRO BO 132969-60-9
NTE Swern oxidation

RX(16) RCT BO 132969-60-9, BP 77877-20-4
RGT V 121-44-8 Et3N, F 60669-69-4 F3CSO3BBu2
PRO BQ 132969-62-1

RX(17) RCT BQ 132969-62-1, BR 6638-79-5
RGT BT 75-24-1 AlMe3
PRO BS 252342-49-7
SOL 109-99-9 THF
NTE yield over 5 steps starting from Roche's ester = 72%

RX(24) RCT BS 252342-49-7, L 69739-34-0

STAGE(1)
RGT N 108-48-5 2,6-Lutidine

STAGE(2)
RGT CG 1333-74-0 H2
CAT 12135-22-7 Pd(OH)2
SOL 64-17-5 EtOH

STAGE(3)
RGT U 26412-87-3 Pyridine-SO3 (1:1), E 7087-68-5 EtN(Pr-i)2

PRO CF 252342-42-0

RX(25) RCT CF 252342-42-0

STAGE(1)
RGT CK 7550-45-0 TiCl4
SOL 75-09-2 CH2Cl2

STAGE(2)
 RCT CI 130043-07-1
 CON -78 deg C

STAGE(3)
 RGT CL 76-05-1 F3CCO2H
 SOL 110-54-3 Hexane
 CON room temperature

PRO CJ 252342-43-1

RX(33) RCT CJ 252342-43-1
 RGT CW 54575-49-4 K Selectride
 PRO CM 256920-77-1
 SOL 109-99-9 THF, 108-88-3 PhMe
 NTE stereoselective, ratio of diastereomers = 9:1

RX(26) RCT CM 256920-77-1, L 69739-34-0

STAGE(1)
 SOL 75-09-2 CH2Cl2

STAGE(2)
 RGT AJ 10028-15-6 Ozone
 SOL 75-09-2 CH2Cl2

STAGE(3)
 RGT BE 603-35-0 PPh3

PRO CN 252342-51-1
 NTE yield over 12 steps starting from Roche's ester = 33%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
 RGT CA 1070-89-9 (Me3Si)2N.Na
 PRO AW 850211-74-4
 CON -78 deg C -> -10 deg C
 NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)
 RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
 SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0 Pentane
 CON SUBSTAGE(1) room temperature -> -78 deg C
 SUBSTAGE(2) -78 deg C
 SUBSTAGE(3) -78 deg C -> room temperature
 SUBSTAGE(4) 1 hour, room temperature

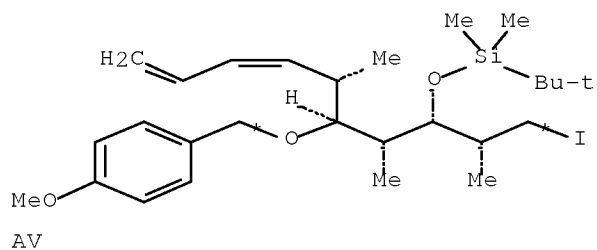
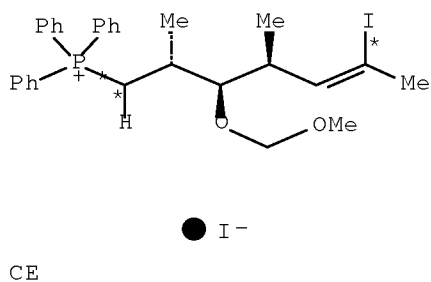
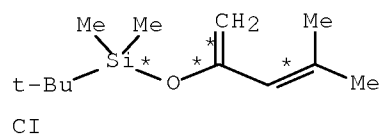
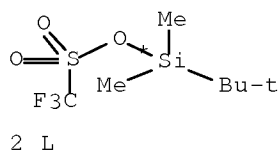
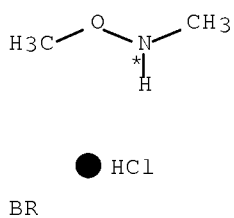
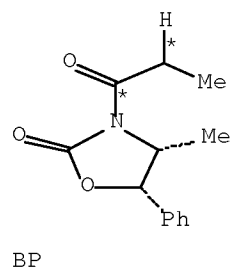
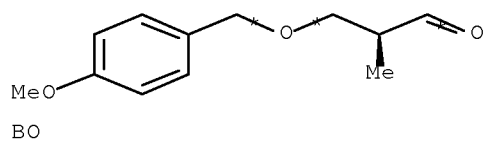
STAGE(2)
 RCT AW 850211-74-4
 RGT BA 534-17-8 Cs2CO3
 CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

PRO AX 633293-75-1
 NTE BBN related byproducts were obtained in 10% yield, Suzuki

coupling

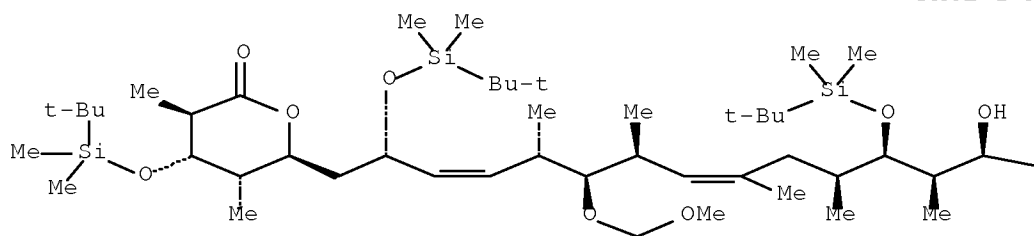
RX(310) OF 354 COMPOSED OF RX(16), RX(17), RX(24), RX(25), RX(33), RX(26),
RX(27), RX(11), RX(28)

RX(310) BO + BP + BR + 2 L + CI + CE + AV
====> CO

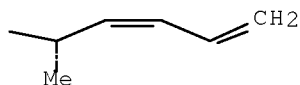


9
STEPS
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PAGE 1-A



PAGE 1-B



CO
YIELD 91%

RX(16) RCT BO 132969-60-9, BP 77877-20-4
RGT V 121-44-8 Et3N, F 60669-69-4 F3CSO3BBu2
PRO BQ 132969-62-1

RX(17) RCT BQ 132969-62-1, BR 6638-79-5
RGT BT 75-24-1 AlMe3
PRO BS 252342-49-7
SOL 109-99-9 THF
NTE yield over 5 steps starting from Roche's ester = 72%

RX(24) RCT BS 252342-49-7, L 69739-34-0

STAGE(1)
RGT N 108-48-5 2,6-Lutidine

STAGE(2)
RGT CG 1333-74-0 H2
CAT 12135-22-7 Pd(OH)2
SOL 64-17-5 EtOH

STAGE(3)
RGT U 26412-87-3 Pyridine-SO3 (1:1), E 7087-68-5 EtN(Pr-i)2

PRO CF 252342-42-0

RX(25) RCT CF 252342-42-0

STAGE(1)
RGT CK 7550-45-0 TiCl4
SOL 75-09-2 CH2Cl2

STAGE(2)
RCT CI 130043-07-1
CON -78 deg C

STAGE(3)
RGT CL 76-05-1 F3CCO2H
SOL 110-54-3 Hexane
CON room temperature

PRO CJ 252342-43-1

RX(33) RCT CJ 252342-43-1
RGT CW 54575-49-4 K Selectride
PRO CM 256920-77-1
SOL 109-99-9 THF, 108-88-3 PhMe
NTE stereoselective, ratio of diastereomers = 9:1

RX(26) RCT CM 256920-77-1, L 69739-34-0

STAGE(1)
SOL 75-09-2 CH2Cl2

STAGE(2)
RGT AJ 10028-15-6 Ozone
SOL 75-09-2 CH2Cl2

STAGE(3)
RGT BE 603-35-0 PPh3

PRO CN 252342-51-1
NTE yield over 12 steps starting from Roche's ester = 33%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
RGT CA 1070-89-9 (Me3Si)2N.Na
PRO AW 850211-74-4
CON -78 deg C -> -10 deg C
NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)
RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0 Pentane
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) -78 deg C
SUBSTAGE(3) -78 deg C -> room temperature
SUBSTAGE(4) 1 hour, room temperature

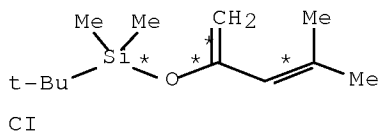
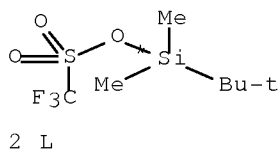
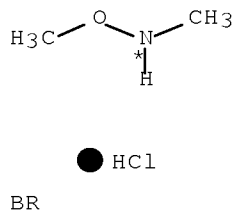
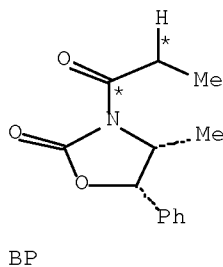
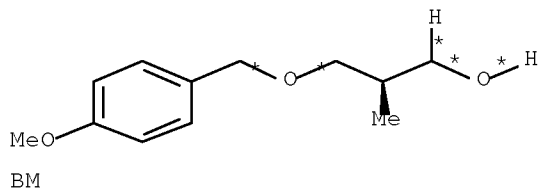
STAGE(2)
RCT AW 850211-74-4
RGT BA 534-17-8 Cs2CO3
CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,

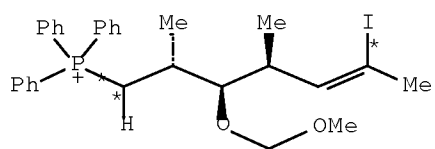
(SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

PRO AX 633293-75-1
 NTE BBN related byproducts were obtained in 10% yield, Suzuki
 coupling

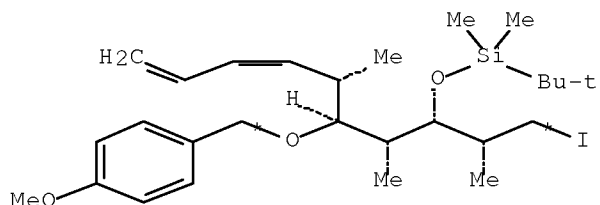
RX(28) RCT AX 633293-75-1
 RGT CC 84-58-2 DDQ
 PRO CO 633293-76-2
 SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
 CON 0 - room temperature deg C

RX(312) OF 354 COMPOSED OF RX(15), RX(16), RX(17), RX(24), RX(25), RX(33),
 RX(26), RX(27), RX(11), RX(28)
 RX(312) BM + BP + BR + 2 L + CI + CE + AV
 ==> CO





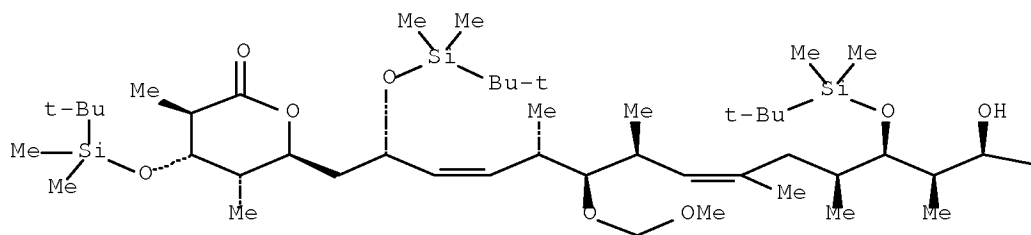
CE



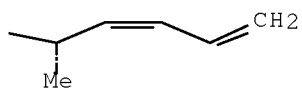
AV

10
STEPS
→

PAGE 1-A



PAGE 1-B



CO
YIELD 91%

RX(15) RCT BM 136320-64-4
PRO BO 132969-60-9
NTE Swern oxidation

RX(16) RCT BO 132969-60-9, BP 77877-20-4

RGT V 121-44-8 Et3N, F 60669-69-4 F3CSO3BBu2
 PRO BQ 132969-62-1

RX(17) RCT BQ 132969-62-1, BR 6638-79-5
 RGT BT 75-24-1 AlMe3
 PRO BS 252342-49-7
 SOL 109-99-9 THF
 NTE yield over 5 steps starting from Roche's ester = 72%

RX(24) RCT BS 252342-49-7, L 69739-34-0

STAGE(1)
 RGT N 108-48-5 2,6-Lutidine

STAGE(2)
 RGT CG 1333-74-0 H2
 CAT 12135-22-7 Pd(OH)2
 SOL 64-17-5 EtOH

STAGE(3)
 RGT U 26412-87-3 Pyridine-SO3 (1:1), E 7087-68-5 EtN(Pr-i)2

PRO CF 252342-42-0

RX(25) RCT CF 252342-42-0

STAGE(1)
 RGT CK 7550-45-0 TiCl4
 SOL 75-09-2 CH2Cl2

STAGE(2)
 RCT CI 130043-07-1
 CON -78 deg C

STAGE(3)
 RGT CL 76-05-1 F3CCO2H
 SOL 110-54-3 Hexane
 CON room temperature

PRO CJ 252342-43-1

RX(33) RCT CJ 252342-43-1
 RGT CW 54575-49-4 K Selectride
 PRO CM 256920-77-1
 SOL 109-99-9 THF, 108-88-3 PhMe
 NTE stereoselective, ratio of diastereomers = 9:1

RX(26) RCT CM 256920-77-1, L 69739-34-0

STAGE(1)
 SOL 75-09-2 CH2Cl2

STAGE(2)
 RGT AJ 10028-15-6 Ozone
 SOL 75-09-2 CH2Cl2

STAGE(3)
 RGT BE 603-35-0 PPh3

PRO CN 252342-51-1

NTE yield over 12 steps starting from Roche's ester = 33%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
RGT CA 1070-89-9 (Me3Si)2N.Na
PRO AW 850211-74-4
CON -78 deg C -> -10 deg C
NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) -78 deg C
SUBSTAGE(3) -78 deg C -> room temperature
SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AW 850211-74-4
RGT BA 534-17-8 Cs2CO3
CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

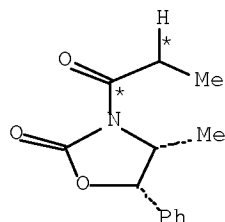
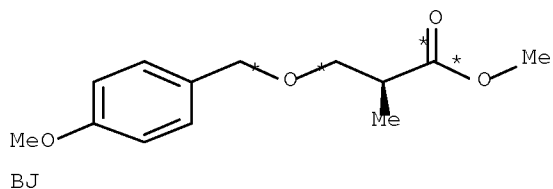
PRO AX 633293-75-1

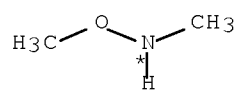
NTE BBN related byproducts were obtained in 10% yield, Suzuki
coupling

RX(28) RCT AX 633293-75-1
RGT CC 84-58-2 DDQ
PRO CO 633293-76-2
SOL 7732-18-5 Water, 75-09-2 CH2Cl2
CON 0 - room temperature deg C

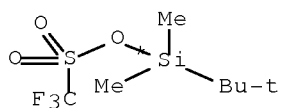
RX(314) OF 354 COMPOSED OF RX(14), RX(15), RX(16), RX(17), RX(24), RX(25),
RX(33), RX(26), RX(27), RX(11), RX(28)

RX(314) BJ + BP + BR + 2 L + CI + CE + AV
====> CO

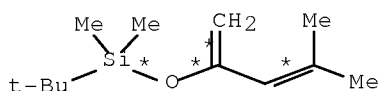




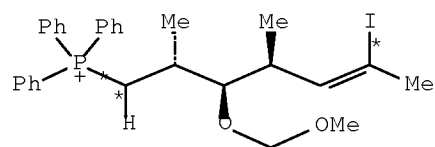
BR



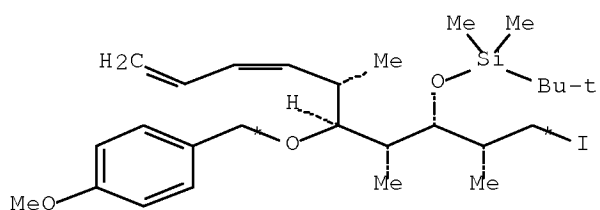
2 L



CI



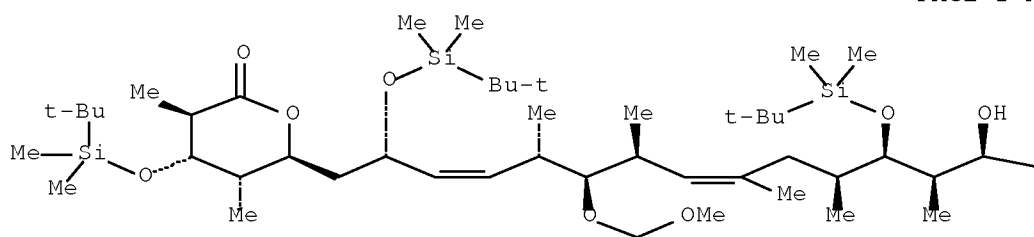
CE

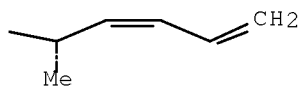


AV

11
STEPS
→

PAGE 1-A





CO
YIELD 91%

RX(14) RCT BJ 132969-71-2
RGT BN 16853-85-3 LiAlH₄
PRO BM 136320-64-4
SOL 109-99-9 THF

RX(15) RCT BM 136320-64-4
PRO BO 132969-60-9
NTE Swern oxidation

RX(16) RCT BO 132969-60-9, BP 77877-20-4
RGT V 121-44-8 Et₃N, F 60669-69-4 F₃CSO₃BBu₂
PRO BQ 132969-62-1

RX(17) RCT BQ 132969-62-1, BR 6638-79-5
RGT BT 75-24-1 AlMe₃
PRO BS 252342-49-7
SOL 109-99-9 THF
NTE yield over 5 steps starting from Roche's ester = 72%

RX(24) RCT BS 252342-49-7, L 69739-34-0

STAGE(1)
RGT N 108-48-5 2,6-Lutidine

STAGE(2)
RGT CG 1333-74-0 H₂
CAT 12135-22-7 Pd(OH)₂
SOL 64-17-5 EtOH

STAGE(3)
RGT U 26412-87-3 Pyridine-SO₃ (1:1), E 7087-68-5 EtN(Pr-i)₂

PRO CF 252342-42-0

RX(25) RCT CF 252342-42-0

STAGE(1)
RGT CK 7550-45-0 TiCl₄
SOL 75-09-2 CH₂Cl₂

STAGE(2)
RCT CI 130043-07-1
CON -78 deg C

STAGE(3)
 RGT CL 76-05-1 F3CCO2H
 SOL 110-54-3 Hexane
 CON room temperature

 PRO CJ 252342-43-1

 RX(33) RCT CJ 252342-43-1
 RGT CW 54575-49-4 K Selectride
 PRO CM 256920-77-1
 SOL 109-99-9 THF, 108-88-3 PhMe
 NTE stereoselective, ratio of diastereomers = 9:1

 RX(26) RCT CM 256920-77-1, L 69739-34-0

 STAGE(1)
 SOL 75-09-2 CH2Cl2

 STAGE(2)
 RGT AJ 10028-15-6 Ozone
 SOL 75-09-2 CH2Cl2

 STAGE(3)
 RGT BE 603-35-0 PPh3

 PRO CN 252342-51-1
 NTE yield over 12 steps starting from Roche's ester = 33%

 RX(27) RCT CE 850211-72-2, CN 252342-51-1
 RGT CA 1070-89-9 (Me3Si)2N.Na
 PRO AW 850211-74-4
 CON -78 deg C -> -10 deg C
 NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

 RX(11) RCT AV 850211-69-7

 STAGE(1)
 RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
 SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
 Pentane
 CON SUBSTAGE(1) room temperature -> -78 deg C
 SUBSTAGE(2) -78 deg C
 SUBSTAGE(3) -78 deg C -> room temperature
 SUBSTAGE(4) 1 hour, room temperature

 STAGE(2)
 RCT AW 850211-74-4
 RGT BA 534-17-8 Cs2CO3
 CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

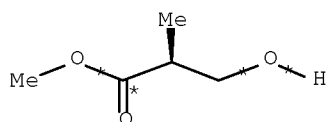
 PRO AX 633293-75-1
 NTE BBN related byproducts were obtained in 10% yield, Suzuki
 coupling

 RX(28) RCT AX 633293-75-1
 RGT CC 84-58-2 DDQ

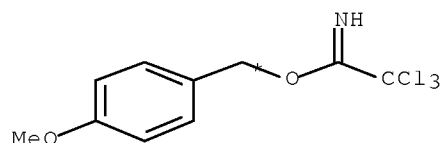
PRO CO 633293--76--2
 SOL 7732-18-5 Water, 75-09-2 CH2Cl2
 CON 0 - room temperature deg C

RX(316) OF 354 COMPOSED OF RX(13), RX(14), RX(15), RX(16), RX(17), RX(24),
 RX(25), RX(33), RX(26), RX(27), RX(11), RX(28)

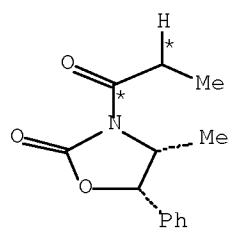
RX(316) BI + AD + BP + BR + 2 L + CI + CE +
 AV ==> CO



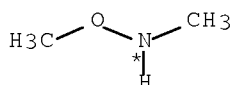
BI



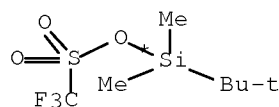
AD



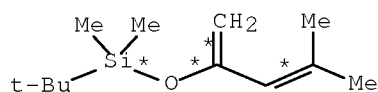
BP



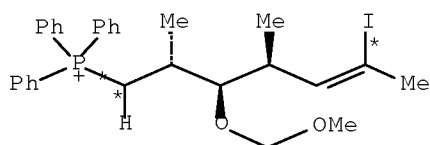
BR



2 L

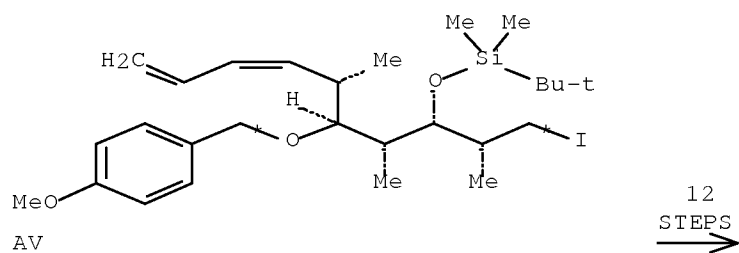


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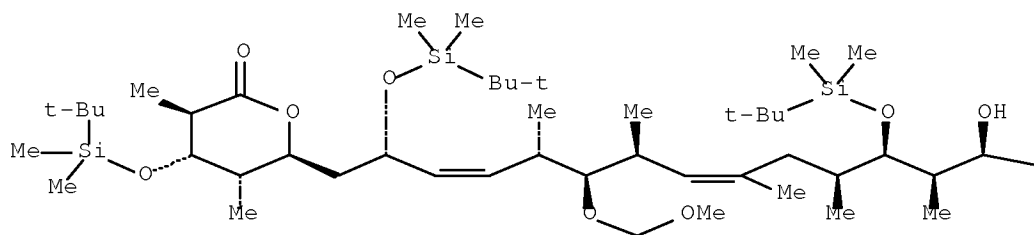


CE

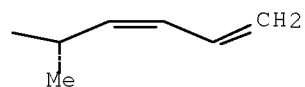




PAGE 1-A



PAGE 1-B



CO
YIELD 91%

RX(13)	RCT	BI 80657-57-4, AD 89238-99-3
	RGT	BK 24057-28-1 Pyridinium tosylate
	PRO	BJ 132969-71-2
	SOL	75-09-2 CH ₂ Cl ₂ , 110-82-7 Cyclohexane
RX(14)	RCT	BJ 132969-71-2
	RGT	BN 16853-85-3 LiAlH ₄
	PRO	BM 136320-64-4
	SOL	109-99-9 THF
RX(15)	RCT	BM 136320-64-4
	PRO	BO 132969-60-9
	NTE	Swern oxidation

RX(16) RCT BO 132969-60-9, BP 77877-20-4
 RGT V 121-44-8 Et3N, F 60669-69-4 F3CSO3BBu2
 PRO BQ 132969-62-1

RX(17) RCT BQ 132969-62-1, BR 6638-79-5
 RGT BT 75-24-1 AlMe3
 PRO BS 252342-49-7
 SOL 109-99-9 THF
 NTE yield over 5 steps starting from Roche's ester = 72%

RX(24) RCT BS 252342-49-7, L 69739-34-0

 STAGE(1)
 RGT N 108-48-5 2,6-Lutidine

 STAGE(2)
 RGT CG 1333-74-0 H2
 CAT 12135-22-7 Pd(OH)2
 SOL 64-17-5 EtOH

 STAGE(3)
 RGT U 26412-87-3 Pyridine-SO3 (1:1), E 7087-68-5 EtN(Pr-i)2

 PRO CF 252342-42-0

RX(25) RCT CF 252342-42-0

 STAGE(1)
 RGT CK 7550-45-0 TiCl4
 SOL 75-09-2 CH2Cl2

 STAGE(2)
 RCT CI 130043-07-1
 CON -78 deg C

 STAGE(3)
 RGT CL 76-05-1 F3CCO2H
 SOL 110-54-3 Hexane
 CON room temperature

 PRO CJ 252342-43-1

RX(33) RCT CJ 252342-43-1
 RGT CW 54575-49-4 K Selectride
 PRO CM 256920-77-1
 SOL 109-99-9 THF, 108-88-3 PhMe
 NTE stereoselective, ratio of diastereomers = 9:1

RX(26) RCT CM 256920-77-1, L 69739-34-0

 STAGE(1)
 SOL 75-09-2 CH2Cl2

 STAGE(2)
 RGT AJ 10028-15-6 Ozone
 SOL 75-09-2 CH2Cl2

 STAGE(3)
 RGT BE 603-35-0 PPh3

PRO CN 252342-51-1
NTE yield over 12 steps starting from Roche's ester = 33%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
RGT CA 1070-89-9 (Me3Si)2N.Na
PRO AW 850211-74-4
CON -78 deg C -> -10 deg C
NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) -78 deg C
SUBSTAGE(3) -78 deg C -> room temperature
SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

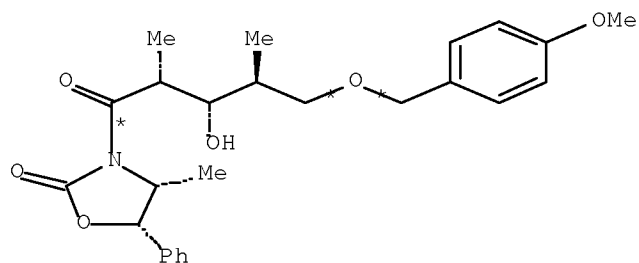
RCT AW 850211-74-4
RGT BA 534-17-8 Cs2CO3
CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

PRO AX 633293-75-1
NTE BBN related byproducts were obtained in 10% yield, Suzuki
coupling

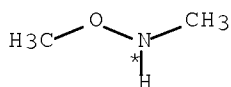
RX(28) RCT AX 633293-75-1
RGT CC 84-58-2 DDQ
PRO CO 633293-76-2
SOL 7732-18-5 Water, 75-09-2 CH2Cl2
CON 0 - room temperature deg C

RX(318) OF 354 COMPOSED OF RX(17), RX(24), RX(25), RX(33), RX(26), RX(27),
RX(11), RX(28), RX(29)

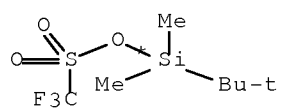
RX(318) BQ + BR + 2 L + CI + CE + AV + CP
====> CQ



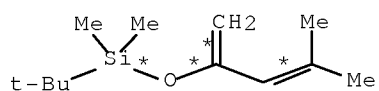
BQ



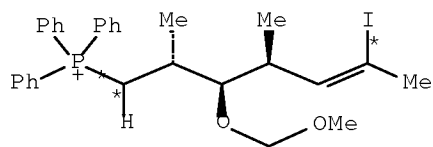
BR



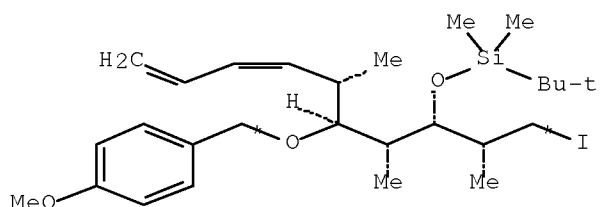
2 L



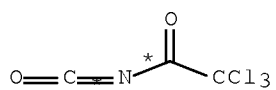
CI



CE



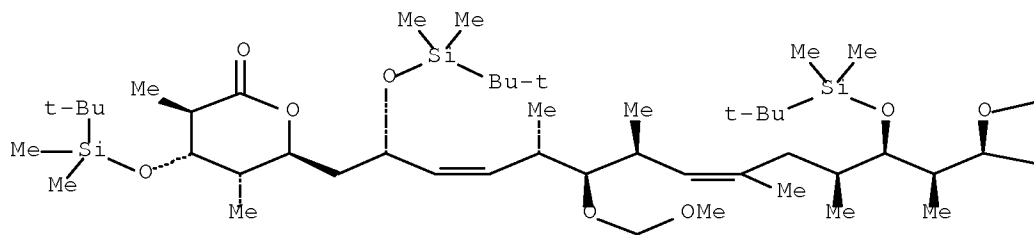
AV

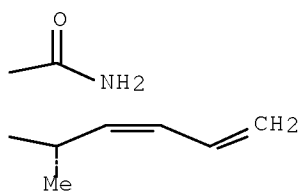


CP

9
STEPS
→

PAGE 1-A





CO
YIELD 92%

```

RX(17)      RCT  BQ 132969-62-1, BR 6638-79-5
            RGT  BT 75-24-1 AlMe3
            PRO  BS 252342-49-7
            SOL  109-99-9 THF
            NTE  yield over 5 steps starting from Roche's ester = 72%

RX(24)      RCT  BS 252342-49-7, L 69739-34-0

            STAGE(1)
              RGT  N 108-48-5 2,6-Lutidine

            STAGE(2)
              RGT  CG 1333-74-0 H2
              CAT  12135-22-7 Pd(OH)2
              SOL  64-17-5 EtOH

            STAGE(3)
              RGT  U 26412-87-3 Pyridine-SO3 (1:1), E 7087-68-5 EtN(Pr-i)2

            PRO  CF 252342-42-0

RX(25)      RCT  CF 252342-42-0

            STAGE(1)
              RGT  CK 7550-45-0 TiCl4
              SOL  75-09-2 CH2Cl2

            STAGE(2)
              RCT  CI 130043-07-1
              CON  -78 deg C

            STAGE(3)
              RGT  CL 76-05-1 F3CCO2H
              SOL  110-54-3 Hexane
              CON  room temperature

            PRO  CJ 252342-43-1

RX(33)      RCT  CJ 252342-43-1
            RGT  CW 54575-49-4 K Selectride
            PRO  CM 256920-77-1
            SOL  109-99-9 THF, 108-88-3 PhMe
            NTE  stereoselective, ratio of diastereomers = 9:1
  
```

RX(26) RCT CM 256920-77-1, L 69739-34-0

STAGE(1)
SOL 75-09-2 CH2Cl2

STAGE(2)
RGT AJ 10028-15-6 Ozone
SOL 75-09-2 CH2Cl2

STAGE(3)
RGT BE 603-35-0 PPh3

PRO CN 252342-51-1
NTE yield over 12 steps starting from Roche's ester = 33%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
RGT CA 1070-89-9 (Me3Si)2N.Na
PRO AW 850211-74-4
CON -78 deg C -> -10 deg C
NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)
RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0 Pentane
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) -78 deg C
SUBSTAGE(3) -78 deg C -> room temperature
SUBSTAGE(4) 1 hour, room temperature

STAGE(2)
RCT AW 850211-74-4
RGT BA 534-17-8 Cs2CO3
CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

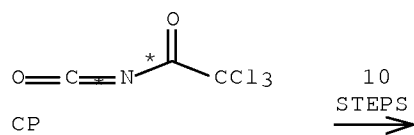
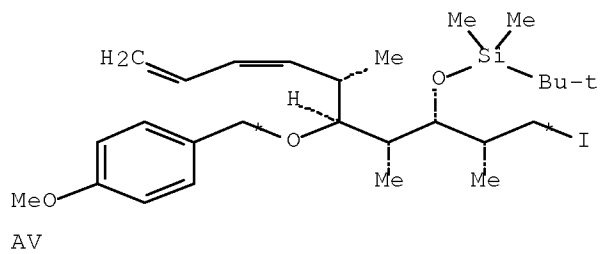
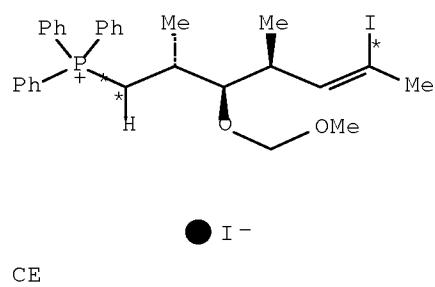
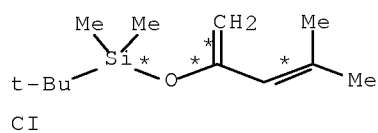
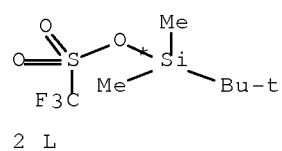
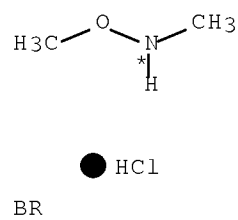
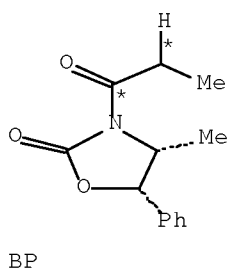
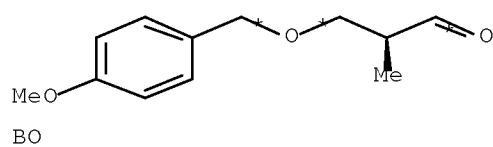
PRO AX 633293-75-1
NTE BBN related byproducts were obtained in 10% yield, Suzuki coupling

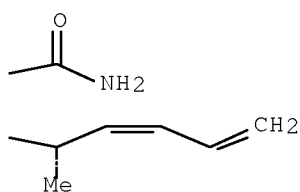
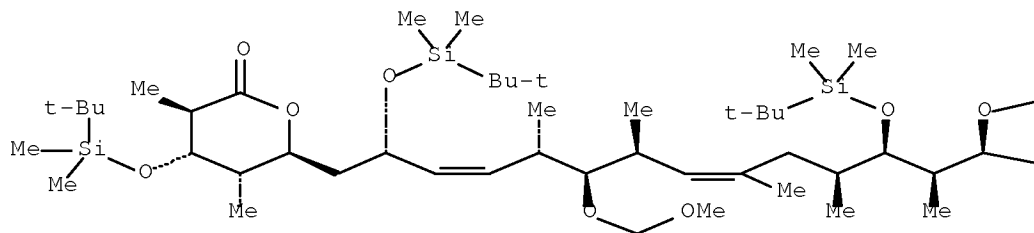
RX(28) RCT AX 633293-75-1
RGT CC 84-58-2 DDQ
PRO CO 633293-76-2
SOL 7732-18-5 Water, 75-09-2 CH2Cl2
CON 0 - room temperature deg C

RX(29) RCT CO 633293-76-2, CP 3019-71-4
RGT CR 1344-28-1 Al2O3
PRO CQ 633293-93-3

RX(320) OF 354 COMPOSED OF RX(16), RX(17), RX(24), RX(25), RX(33), RX(26),
RX(27), RX(11), RX(28), RX(29)

RX(320) BO + BP + BR + 2 L + CI + CE + AV +
CP ==> CQ





CO
YIELD 92%

RX(16) RCT BO 132969-60-9, BP 77877-20-4
RGT V 121-44-8 Et3N, F 60669-69-4 F3CSO3BBu2
PRO BQ 132969-62-1

RX(17) RCT BQ 132969-62-1, BR 6638-79-5
RGT BT 75-24-1 AlMe3
PRO BS 252342-49-7
SOL 109-99-9 THF
NTE yield over 5 steps starting from Roche's ester = 72%

RX(24) RCT BS 252342-49-7, L 69739-34-0

STAGE(1)
RGT N 108-48-5 2,6-Lutidine

STAGE(2)
RGT CG 1333-74-0 H2
CAT 12135-22-7 Pd(OH)2
SOL 64-17-5 EtOH

STAGE(3)
RGT U 26412-87-3 Pyridine-SO3 (1:1), E 7087-68-5 EtN(Pr-i)2

PRO CF 252342-42-0

RX(25) RCT CF 252342-42-0

STAGE(1)
RGT CK 7550-45-0 TiCl4

SOL 75-09-2 CH2Cl2

STAGE(2)

RCT CI 130043-07-1

CON -78 deg C

STAGE(3)

RGT CL 76-05-1 F3CCO2H

SOL 110-54-3 Hexane

CON room temperature

PRO CJ 252342-43-1

RX(33)

RCT CJ 252342-43-1

RGT CW 54575-49-4 K Selectride

PRO CM 256920-77-1

SOL 109-99-9 THF, 108-88-3 PhMe

NTE stereoselective, ratio of diastereomers = 9:1

RX(26)

RCT CM 256920-77-1, L 69739-34-0

STAGE(1)

SOL 75-09-2 CH2Cl2

STAGE(2)

RGT AJ 10028-15-6 Ozone

SOL 75-09-2 CH2Cl2

STAGE(3)

RGT BE 603-35-0 PPh3

PRO CN 252342-51-1

NTE yield over 12 steps starting from Roche's ester = 33%

RX(27)

RCT CE 850211-72-2, CN 252342-51-1

RGT CA 1070-89-9 (Me3Si)2N.Na

PRO AW 850211-74-4

CON -78 deg C -> -10 deg C

NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11)

RCT AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi

SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane

CON SUBSTAGE(1) room temperature -> -78 deg C

SUBSTAGE(2) -78 deg C

SUBSTAGE(3) -78 deg C -> room temperature

SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AW 850211-74-4

RGT BA 534-17-8 Cs2CO3

CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-

SOL 7732-18-5 Water, 68-12-2 DMF

CON 20 hours, room temperature

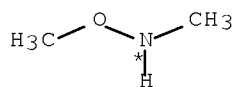
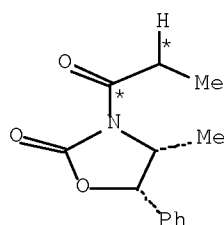
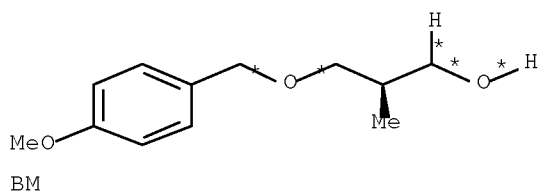
PRO AX 633293-75-1
 NTE BBN related byproducts were obtained in 10% yield, Suzuki coupling

RX(28) RCT AX 633293-75-1
 RGT CC 84-58-2 DDQ
 PRO CO 633293-76-2
 SOL 7732-18-5 Water, 75-09-2 CH2Cl2
 CON 0 - room temperature deg C

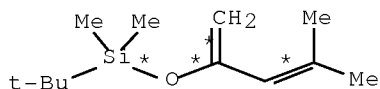
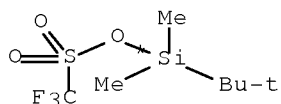
RX(29) RCT CO 633293-76-2, CP 3019-71-4
 RGT CR 1344-28-1 Al2O3
 PRO CQ 633293-93-3

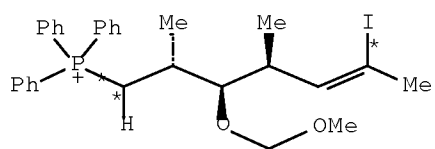
RX(322) OF 354 COMPOSED OF RX(15), RX(16), RX(17), RX(24), RX(25), RX(33),
 RX(26), RX(27), RX(11), RX(28), RX(29)

RX(322) BM + BP + BR + 2 L + CI + CE + AV +
 CP ==> CQ

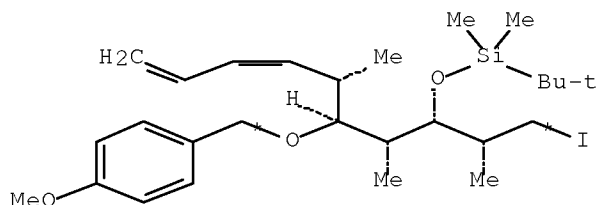


● HCl

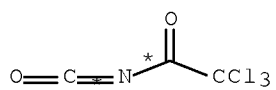




CE



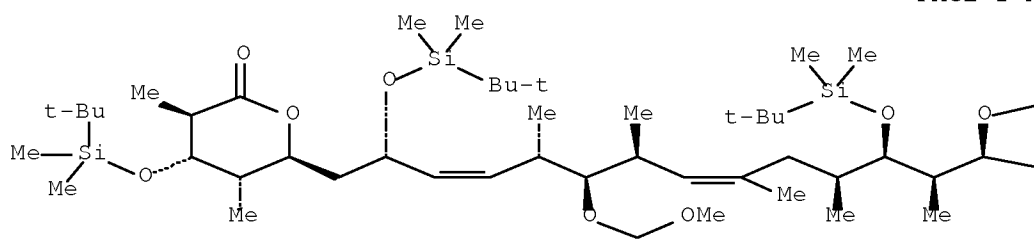
AV



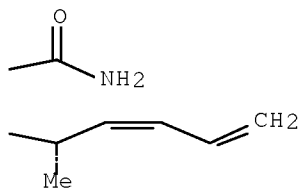
CP

11
STEPS
→

PAGE 1-A



PAGE 1-B



CO
YIELD 92%

RX(15) RCT BM 136320-64-4
PRO BO 132969-60-9

NTE Swern oxidation

RX(16) RCT BO 132969-60-9, BP 77877-20-4
RGT V 121-44-8 Et3N, F 60669-69-4 F3CSO3BBu2
PRO BQ 132969-62-1

RX(17) RCT BQ 132969-62-1, BR 6638-79-5
RGT BT 75-24-1 AlMe3
PRO BS 252342-49-7
SOL 109-99-9 THF
NTE yield over 5 steps starting from Roche's ester = 72%

RX(24) RCT BS 252342-49-7, L 69739-34-0

STAGE(1)
RGT N 108-48-5 2,6-Lutidine

STAGE(2)
RGT CG 1333-74-0 H2
CAT 12135-22-7 Pd(OH)2
SOL 64-17-5 EtOH

STAGE(3)
RGT U 26412-87-3 Pyridine-SO3 (1:1), E 7087-68-5 EtN(Pr-i)2

PRO CF 252342-42-0

RX(25) RCT CF 252342-42-0

STAGE(1)
RGT CK 7550-45-0 TiCl4
SOL 75-09-2 CH2Cl2

STAGE(2)
RCT CI 130043-07-1
CON -78 deg C

STAGE(3)
RGT CL 76-05-1 F3CCO2H
SOL 110-54-3 Hexane
CON room temperature

PRO CJ 252342-43-1

RX(33) RCT CJ 252342-43-1
RGT CW 54575-49-4 K Selectride
PRO CM 256920-77-1
SOL 109-99-9 THF, 108-88-3 PhMe
NTE stereoselective, ratio of diastereomers = 9:1

RX(26) RCT CM 256920-77-1, L 69739-34-0

STAGE(1)
SOL 75-09-2 CH2Cl2

STAGE(2)
RGT AJ 10028-15-6 Ozone
SOL 75-09-2 CH2Cl2

STAGE(3)

RGT BE 603-35-0 PPh3

PRO CN 252342-51-1
 NTE yield over 12 steps starting from Roche's ester = 33%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
 RGT CA 1070-89-9 (Me3Si)2N.Na
 PRO AW 850211-74-4
 CON -78 deg C -> -10 deg C
 NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)
 RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
 SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0 Pentane
 CON SUBSTAGE(1) room temperature -> -78 deg C
 SUBSTAGE(2) -78 deg C
 SUBSTAGE(3) -78 deg C -> room temperature
 SUBSTAGE(4) 1 hour, room temperature

STAGE(2)
 RCT AW 850211-74-4
 RGT BA 534-17-8 Cs2CO3
 CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

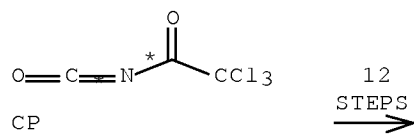
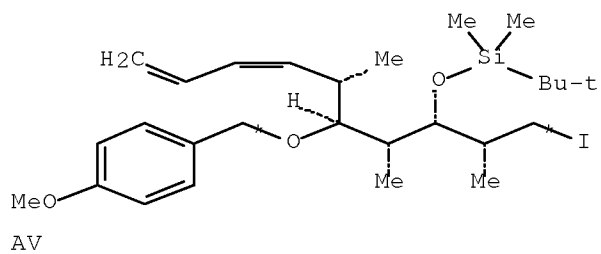
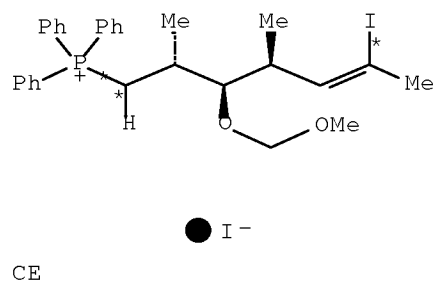
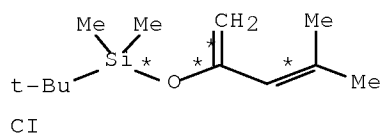
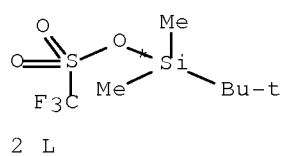
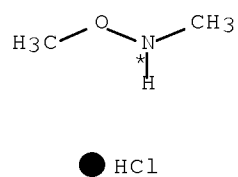
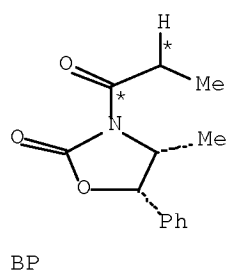
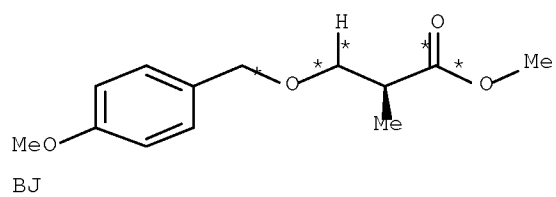
PRO AX 633293-75-1
 NTE BBN related byproducts were obtained in 10% yield, Suzuki coupling

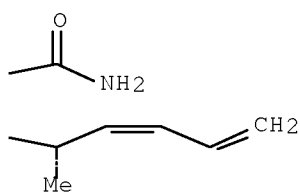
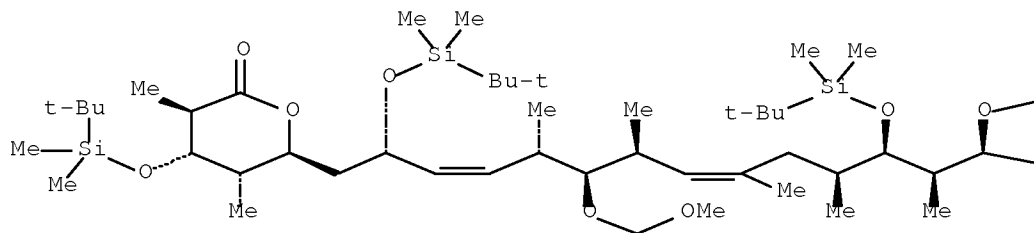
RX(28) RCT AX 633293-75-1
 RGT CC 84-58-2 DDQ
 PRO CO 633293-76-2
 SOL 7732-18-5 Water, 75-09-2 CH2Cl2
 CON 0 - room temperature deg C

RX(29) RCT CO 633293-76-2, CP 3019-71-4
 RGT CR 1344-28-1 Al2O3
 PRO CQ 633293-93-3

RX(324) OF 354 COMPOSED OF RX(14), RX(15), RX(16), RX(17), RX(24), RX(25),
 RX(33), RX(26), RX(27), RX(11), RX(28), RX(29)

RX(324) BJ + BP + BR + 2 L + CI + CE + AV +
 CP ==> CQ





CO
YIELD 92%

RX(14)	RCT	BJ 132969-71-2
	RGT	BN 16853-85-3 LiAlH ₄
	PRO	BM 136320-64-4
	SOL	109-99-9 THF
RX(15)	RCT	BM 136320-64-4
	PRO	BO 132969-60-9
	NTE	Swern oxidation
RX(16)	RCT	BO 132969-60-9, BP 77877-20-4
	RGT	V 121-44-8 Et ₃ N, F 60669-69-4 F ₃ CSO ₃ BBu ₂
	PRO	BQ 132969-62-1
RX(17)	RCT	BQ 132969-62-1, BR 6638-79-5
	RGT	BT 75-24-1 AlMe ₃
	PRO	BS 252342-49-7
	SOL	109-99-9 THF
	NTE	yield over 5 steps starting from Roche's ester = 72%
RX(24)	RCT	BS 252342-49-7, L 69739-34-0
	STAGE(1)	
	RGT	N 108-48-5 2,6-Lutidine
	STAGE(2)	
	RGT	CG 1333-74-0 H ₂
	CAT	12135-22-7 Pd(OH) ₂
	SOL	64-17-5 EtOH

STAGE(3)
 RGT U 26412-87-3 Pyridine-SO3 (1:1), E 7087-68-5 EtN(Pr-i)2
 PRO CF 252342-42-0
 RX(25) RCT CF 252342-42-0
 STAGE(1)
 RGT CK 7550-45-0 TiCl4
 SOL 75-09-2 CH2Cl2
 STAGE(2)
 RCT CI 130043-07-1
 CON -78 deg C
 STAGE(3)
 RGT CL 76-05-1 F3CCO2H
 SOL 110-54-3 Hexane
 CON room temperature
 PRO CJ 252342-43-1
 RX(33) RCT CJ 252342-43-1
 RGT CW 54575-49-4 K Selectride
 PRO CM 256920-77-1
 SOL 109-99-9 THF, 108-88-3 PhMe
 NTE stereoselective, ratio of diastereomers = 9:1
 RX(26) RCT CM 256920-77-1, L 69739-34-0
 STAGE(1)
 SOL 75-09-2 CH2Cl2
 STAGE(2)
 RGT AJ 10028-15-6 Ozone
 SOL 75-09-2 CH2Cl2
 STAGE(3)
 RGT BE 603-35-0 PPh3
 PRO CN 252342-51-1
 NTE yield over 12 steps starting from Roche's ester = 33%
 RX(27) RCT CE 850211-72-2, CN 252342-51-1
 RGT CA 1070-89-9 (Me3Si)2N.Na
 PRO AW 850211-74-4
 CON -78 deg C -> -10 deg C
 NTE stereoselective, Wittig coupling, yield over 13 steps = 20%
 RX(11) RCT AV 850211-69-7
 STAGE(1)
 RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
 SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
 Pentane
 CON SUBSTAGE(1) room temperature -> -78 deg C
 SUBSTAGE(2) -78 deg C
 SUBSTAGE(3) -78 deg C -> room temperature
 SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AW 850211-74-4
 RGT BA 534-17-8 Cs2CO3
 CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

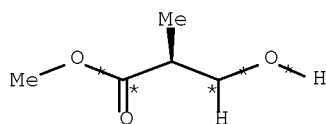
PRO AX 633293-75-1
 NTE BBN related byproducts were obtained in 10% yield, Suzuki
 coupling

RX(28) RCT AX 633293-75-1
 RGT CC 84-58-2 DDQ
 PRO CO 633293-76-2
 SOL 7732-18-5 Water, 75-09-2 CH2Cl2
 CON 0 - room temperature deg C

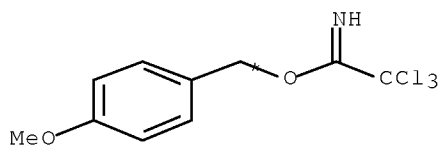
RX(29) RCT CO 633293-76-2, CP 3019-71-4
 RGT CR 1344-28-1 Al2O3
 PRO CQ 633293-93-3

RX(326) OF 354 COMPOSED OF RX(13), RX(14), RX(15), RX(16), RX(17), RX(24),
 RX(25), RX(33), RX(26), RX(27), RX(11), RX(28), RX(29)

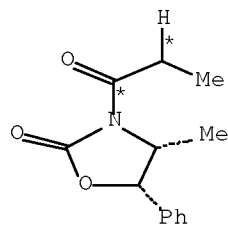
RX(326) BI + AD + BP + BR + 2 L + CI + CE +
 AV + CP ==> CQ



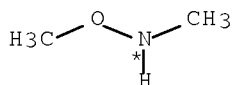
BI



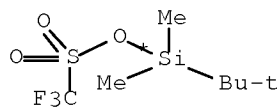
AD



BP



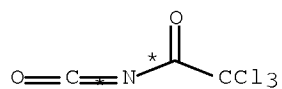
BR



2 L



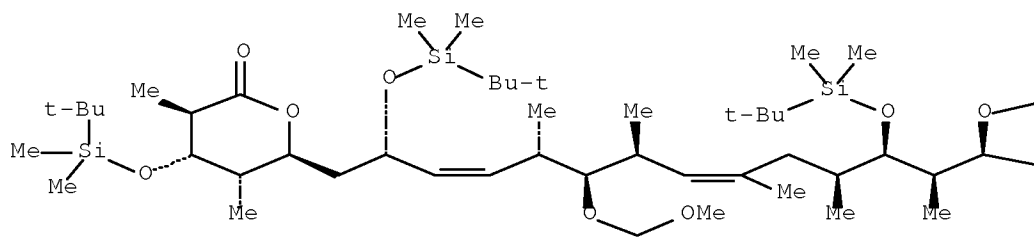
Chemical structure of compound 10: A 4-methoxybenzyl group is attached to a 1,3-dioxolane ring. The dioxolane ring has a methyl group at the 2-position and a 4-methyl-4-iodopent-1-yn-1-yl group at the 3-position. The pentynyl group is shown with stereochemistry: the methyl group at the 4-position is dashed, and the iodine atom is wedged.

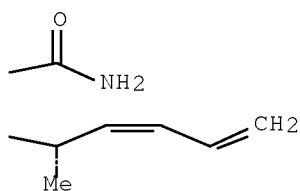


CP

13
STEPS
→

PAGE 1-A





CO
YIELD 92%

RX(13) RCT BI 80657-57-4, AD 89238-99-3
RGT BK 24057-28-1 Pyridinium tosylate
PRO BJ 132969-71-2
SOL 75-09-2 CH₂Cl₂, 110-82-7 Cyclohexane

RX(14) RCT BJ 132969-71-2
RGT BN 16853-85-3 LiAlH₄
PRO BM 136320-64-4
SOL 109-99-9 THF

RX(15) RCT BM 136320-64-4
PRO BO 132969-60-9
NTE Swern oxidation

RX(16) RCT BO 132969-60-9, BP 77877-20-4
RGT V 121-44-8 Et₃N, F 60669-69-4 F₃CSO₃BBu₂
PRO BQ 132969-62-1

RX(17) RCT BQ 132969-62-1, BR 6638-79-5
RGT BT 75-24-1 AlMe₃
PRO BS 252342-49-7
SOL 109-99-9 THF
NTE yield over 5 steps starting from Roche's ester = 72%

RX(24) RCT BS 252342-49-7, L 69739-34-0

STAGE(1)
RGT N 108-48-5 2,6-Lutidine

STAGE(2)
RGT CG 1333-74-0 H₂
CAT 12135-22-7 Pd(OH)₂
SOL 64-17-5 EtOH

STAGE(3)
RGT U 26412-87-3 Pyridine-SO₃ (1:1), E 7087-68-5 EtN(Pr-i)₂

PRO CF 252342-42-0

RX(25) RCT CF 252342-42-0

STAGE(1)
RGT CK 7550-45-0 TiCl₄
SOL 75-09-2 CH₂Cl₂

STAGE(2)
 RCT CI 130043-07-1
 CON -78 deg C

STAGE(3)
 RGT CL 76-05-1 F3CCO2H
 SOL 110-54-3 Hexane
 CON room temperature

PRO CJ 252342-43-1

RX(33) RCT CJ 252342-43-1
 RGT CW 54575-49-4 K Selectride
 PRO CM 256920-77-1
 SOL 109-99-9 THF, 108-88-3 PhMe
 NTE stereoselective, ratio of diastereomers = 9:1

RX(26) RCT CM 256920-77-1, L 69739-34-0

STAGE(1)
 SOL 75-09-2 CH2Cl2

STAGE(2)
 RGT AJ 10028-15-6 Ozone
 SOL 75-09-2 CH2Cl2

STAGE(3)
 RGT BE 603-35-0 PPh3

PRO CN 252342-51-1
 NTE yield over 12 steps starting from Roche's ester = 33%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
 RGT CA 1070-89-9 (Me3Si)2N.Na
 PRO AW 850211-74-4
 CON -78 deg C -> -10 deg C
 NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)
 RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
 SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0 Pentane
 CON SUBSTAGE(1) room temperature -> -78 deg C
 SUBSTAGE(2) -78 deg C
 SUBSTAGE(3) -78 deg C -> room temperature
 SUBSTAGE(4) 1 hour, room temperature

STAGE(2)
 RCT AW 850211-74-4
 RGT BA 534-17-8 Cs2CO3
 CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

PRO AX 633293-75-1

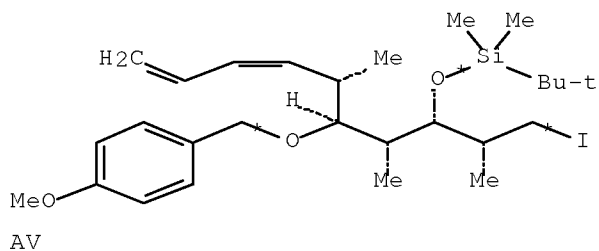
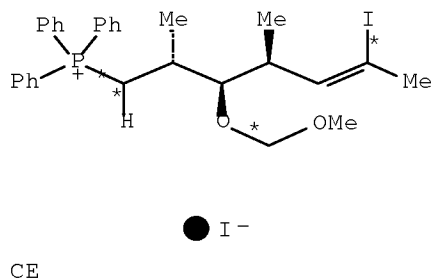
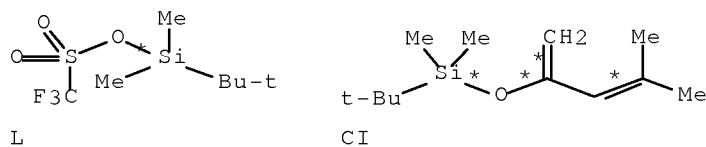
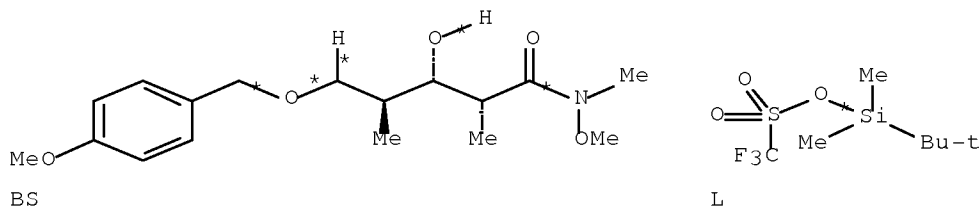
NTE BBN related byproducts were obtained in 10% yield, Suzuki coupling

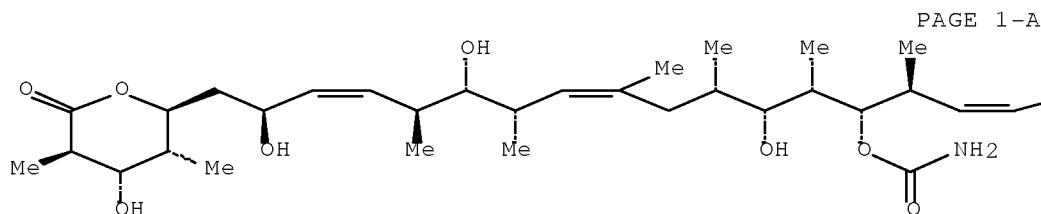
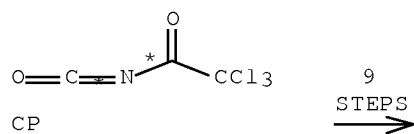
RX(28) RCT AX 633293-75-1
 RGT CC 84-58-2 DDQ
 PRO CO 633293-76-2
 SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
 CON 0 - room temperature deg C

RX(29) RCT CO 633293-76-2, CP 3019-71-4
 RGT CR 1344-28-1 Al₂O₃
 PRO CQ 633293-93-3

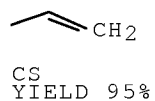
RX(348) OF 354 COMPOSED OF RX(24), RX(25), RX(33), RX(26), RX(27), RX(11),
 RX(28), RX(29), RX(30)

RX(348) BS + 2 L + CI + CE + AV + CP ==>
 CS





PAGE 1-B



RX(24) RCT BS 252342-49-7, L 69739-34-0

STAGE(1)

RGT N 108-48-5 2,6-Lutidine

STAGE(2)

RGT CG 1333-74-0 H2

CAT 12135-22-7 Pd(OH)2

SOL 64-17-5 EtOH

STAGE(3)

RGT U 26412-87-3 Pyridine-SO3 (1:1), E 7087-68-5 EtN(Pr-i)2

PRO CF 252342-42-0

RX(25) RCT CF 252342-42-0

STAGE(1)

RGT CK 7550-45-0 TiCl4

SOL 75-09-2 CH2Cl2

STAGE(2)

RCT CI 130043-07-1

CON -78 deg C

STAGE(3)
 RGT CL 76-05-1 F3CCO2H
 SOL 110-54-3 Hexane
 CON room temperature

 PRO CJ 252342-43-1

 RX(33) RCT CJ 252342-43-1
 RGT CW 54575-49-4 K Selectride
 PRO CM 256920-77-1
 SOL 109-99-9 THF, 108-88-3 PhMe
 NTE stereoselective, ratio of diastereomers = 9:1

 RX(26) RCT CM 256920-77-1, L 69739-34-0

 STAGE(1)
 SOL 75-09-2 CH2Cl2

 STAGE(2)
 RGT AJ 10028-15-6 Ozone
 SOL 75-09-2 CH2Cl2

 STAGE(3)
 RGT BE 603-35-0 PPh3

 PRO CN 252342-51-1
 NTE yield over 12 steps starting from Roche's ester = 33%

 RX(27) RCT CE 850211-72-2, CN 252342-51-1
 RGT CA 1070-89-9 (Me3Si)2N.Na
 PRO AW 850211-74-4
 CON -78 deg C -> -10 deg C
 NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

 RX(11) RCT AV 850211-69-7

 STAGE(1)
 RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
 SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
 Pentane
 CON SUBSTAGE(1) room temperature -> -78 deg C
 SUBSTAGE(2) -78 deg C
 SUBSTAGE(3) -78 deg C -> room temperature
 SUBSTAGE(4) 1 hour, room temperature

 STAGE(2)
 RCT AW 850211-74-4
 RGT BA 534-17-8 Cs2CO3
 CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

 PRO AX 633293-75-1
 NTE BBN related byproducts were obtained in 10% yield, Suzuki
 coupling

 RX(28) RCT AX 633293-75-1
 RGT CC 84-58-2 DDQ

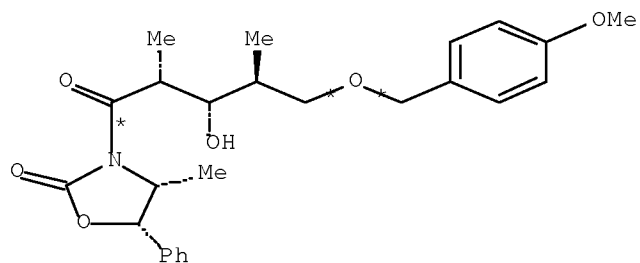
PRO CO 633293-76-2
 SOL 7732-18-5 Water, 75-09-2 CH2Cl2
 CON 0 - room temperature deg C

RX(29) RCT CO 633293-76-2, CP 3019-71-4
 RGT CR 1344-28-1 Al2O3
 PRO CQ 633293-93-3

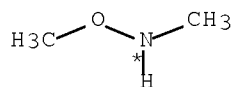
RX(30) RCT CQ 633293-93-3
 RGT CT 7647-01-0 HCl
 PRO CS 127943-53-7
 SOL 7732-18-5 Water, 67-56-1 MeOH
 NTE overall yield via iodine substituted pyran-2-one intermediate = 10%

RX(349) OF 354 COMPOSED OF RX(17), RX(24), RX(25), RX(33), RX(26), RX(27),
 RX(11), RX(28), RX(29), RX(30)

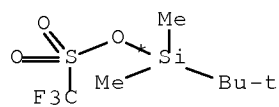
RX(349) BQ + BR + 2 L + CI + CE + AV + CP
 ==> CS



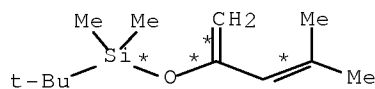
BQ



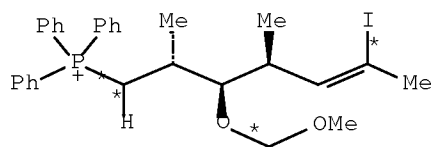
BR



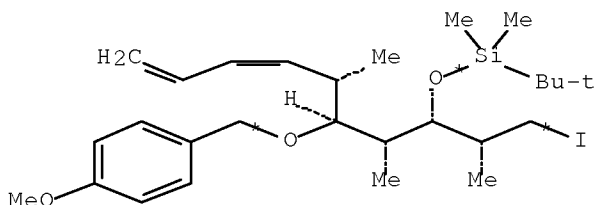
2 L



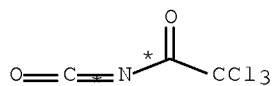
CI



CE

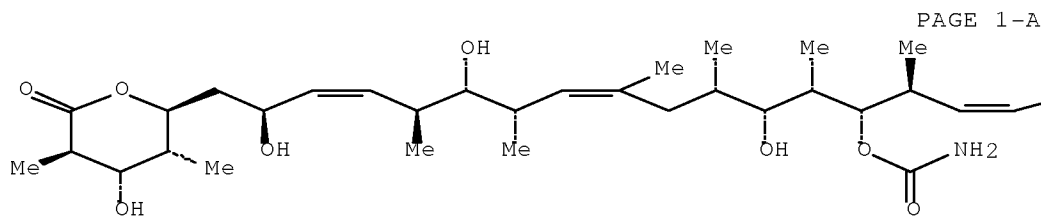


AV

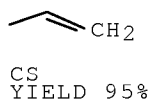


CP

10
STEPS
→



PAGE 1-B



CS
YIELD 95%

RX(17) RCT BQ 132969-62-1, BR 6638-79-5
RGT BT 75-24-1 AlMe3
PRO BS 252342-49-7
SOL 109-99-9 THF
NTE yield over 5 steps starting from Roche's ester = 72%

RX(24) RCT BS 252342-49-7, L 69739-34-0

STAGE(1)

RGT N 108-48-5 2,6-Lutidine

STAGE(2)
 RGT CG 1333-74-0 H2
 CAT 12135-22-7 Pd(OH)2
 SOL 64-17-5 EtOH

STAGE(3)
 RGT U 26412-87-3 Pyridine-SO3 (1:1), E 7087-68-5 EtN(Pr-i)2

PRO CF 252342-42-0

RX(25) RCT CF 252342-42-0

STAGE(1)
 RGT CK 7550-45-0 TiCl4
 SOL 75-09-2 CH2Cl2

STAGE(2)
 RCT CI 130043-07-1
 CON -78 deg C

STAGE(3)
 RGT CL 76-05-1 F3CCO2H
 SOL 110-54-3 Hexane
 CON room temperature

PRO CJ 252342-43-1

RX(33) RCT CJ 252342-43-1
 RGT CW 54575-49-4 K Selectride
 PRO CM 256920-77-1
 SOL 109-99-9 THF, 108-88-3 PhMe
 NTE stereoselective, ratio of diastereomers = 9:1

RX(26) RCT CM 256920-77-1, L 69739-34-0

STAGE(1)
 SOL 75-09-2 CH2Cl2

STAGE(2)
 RGT AJ 10028-15-6 Ozone
 SOL 75-09-2 CH2Cl2

STAGE(3)
 RGT BE 603-35-0 PPh3

PRO CN 252342-51-1
 NTE yield over 12 steps starting from Roche's ester = 33%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
 RGT CA 1070-89-9 (Me3Si)2N.Na
 PRO AW 850211-74-4
 CON -78 deg C -> -10 deg C
 NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)
 RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi

SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) -78 deg C
SUBSTAGE(3) -78 deg C -> room temperature
SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AW 850211-74-4
RGT BA 534-17-8 Cs2CO3
CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

PRO AX 633293-75-1
NTE BBN related byproducts were obtained in 10% yield, Suzuki
coupling

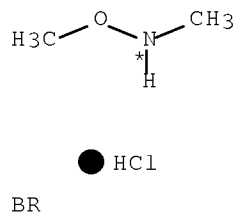
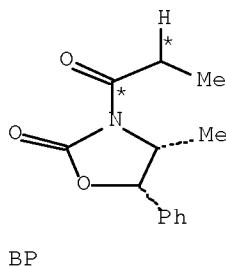
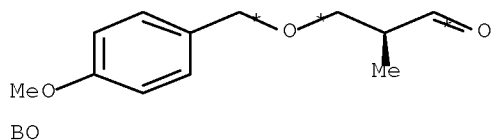
RX(28) RCT AX 633293-75-1
RGT CC 84-58-2 DDQ
PRO CO 633293-76-2
SOL 7732-18-5 Water, 75-09-2 CH2Cl2
CON 0 - room temperature deg C

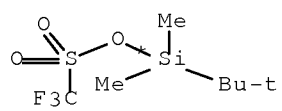
RX(29) RCT CO 633293-76-2, CP 3019-71-4
RGT CR 1344-28-1 Al2O3
PRO CQ 633293-93-3

RX(30) RCT CQ 633293-93-3
RGT CT 7647-01-0 HCl
PRO CS 127943-53-7
SOL 7732-18-5 Water, 67-56-1 MeOH
NTE overall yield via iodine substituted pyran-2-one intermediate =
10%

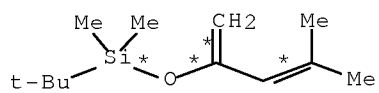
RX(350) OF 354 COMPOSED OF RX(16), RX(17), RX(24), RX(25), RX(33), RX(26),
RX(27), RX(11), RX(28), RX(29), RX(30)

RX(350) BO + BP + BR + 2 L + CI + CE + AV +
CP ==> CS

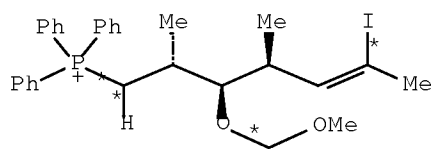




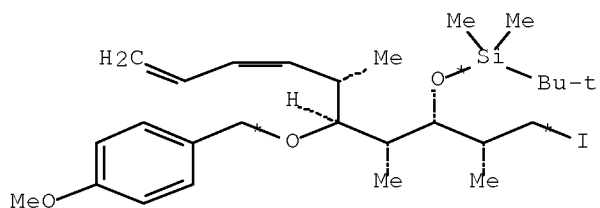
2 L



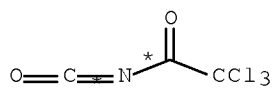
CI



CE

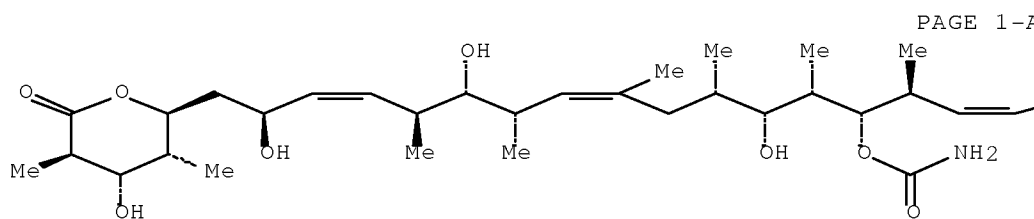


AV



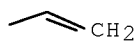
CP

11
STEPS
→



PAGE 1-A

PAGE 1-B



CS
YIELD 95%

RX(16) RCT BO 132969-60-9, BP 77877-20-4
RGT V 121-44-8 Et3N, F 60669-69-4 F3CSO3BBu2
PRO BQ 132969-62-1

RX(17) RCT BQ 132969-62-1, BR 6638-79-5
RGT BT 75-24-1 AlMe3
PRO BS 252342-49-7
SOL 109-99-9 THF
NTE yield over 5 steps starting from Roche's ester = 72%

RX(24) RCT BS 252342-49-7, L 69739-34-0

STAGE(1)
RGT N 108-48-5 2,6-Lutidine

STAGE(2)
RGT CG 1333-74-0 H2
CAT 12135-22-7 Pd(OH)2
SOL 64-17-5 EtOH

STAGE(3)
RGT U 26412-87-3 Pyridine-SO3 (1:1), E 7087-68-5 EtN(Pr-i)2

PRO CF 252342-42-0

RX(25) RCT CF 252342-42-0

STAGE(1)
RGT CK 7550-45-0 TiCl4
SOL 75-09-2 CH2Cl2

STAGE(2)
RCT CI 130043-07-1
CON -78 deg C

STAGE(3)
RGT CL 76-05-1 F3CCO2H
SOL 110-54-3 Hexane
CON room temperature

PRO CJ 252342-43-1

RX(33) RCT CJ 252342-43-1
RGT CW 54575-49-4 K Selectride
PRO CM 256920-77-1
SOL 109-99-9 THF, 108-88-3 PhMe
NTE stereoselective, ratio of diastereomers = 9:1

RX(26) RCT CM 256920-77-1, L 69739-34-0

STAGE(1)
SOL 75-09-2 CH2Cl2

STAGE(2)
RGT AJ 10028-15-6 Ozone
SOL 75-09-2 CH2Cl2

STAGE(3)

RGT BE 603-35-0 PPh3

PRO CN 252342-51-1

NTE yield over 12 steps starting from Roche's ester = 33%

RX(27) RCT CE 850211-72-2, CN 252342-51-1

RGT CA 1070-89-9 (Me3Si)2N.Na

PRO AW 850211-74-4

CON -78 deg C -> -10 deg C

NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi

SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane

CON SUBSTAGE(1) room temperature -> -78 deg C

SUBSTAGE(2) -78 deg C

SUBSTAGE(3) -78 deg C -> room temperature

SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AW 850211-74-4

RGT BA 534-17-8 Cs2CO3

CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-

SOL 7732-18-5 Water, 68-12-2 DMF

CON 20 hours, room temperature

PRO AX 633293-75-1

NTE BBN related byproducts were obtained in 10% yield, Suzuki
coupling

RX(28) RCT AX 633293-75-1

RGT CC 84-58-2 DDQ

PRO CO 633293-76-2

SOL 7732-18-5 Water, 75-09-2 CH2Cl2

CON 0 - room temperature deg C

RX(29) RCT CO 633293-76-2, CP 3019-71-4

RGT CR 1344-28-1 Al2O3

PRO CQ 633293-93-3

RX(30) RCT CQ 633293-93-3

RGT CT 7647-01-0 HCl

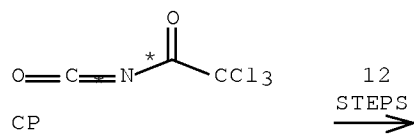
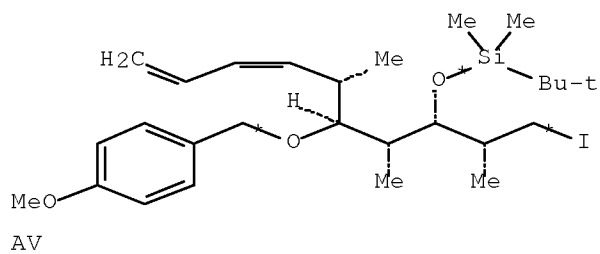
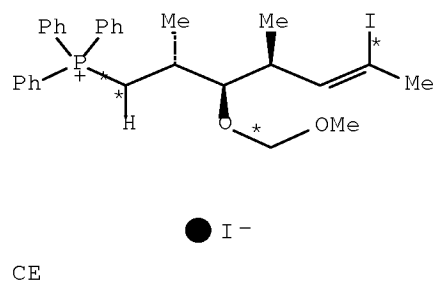
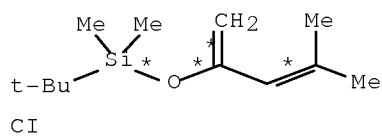
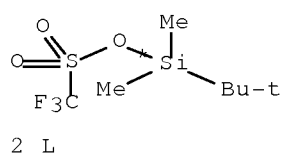
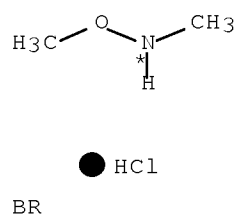
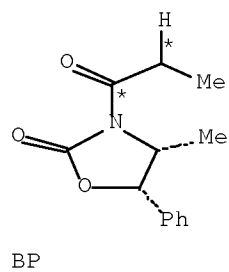
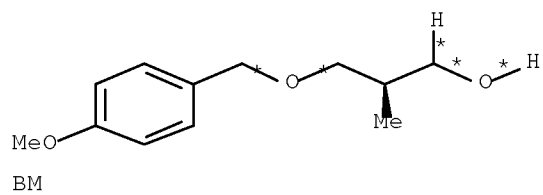
PRO CS 127943-53-7

SOL 7732-18-5 Water, 67-56-1 MeOH

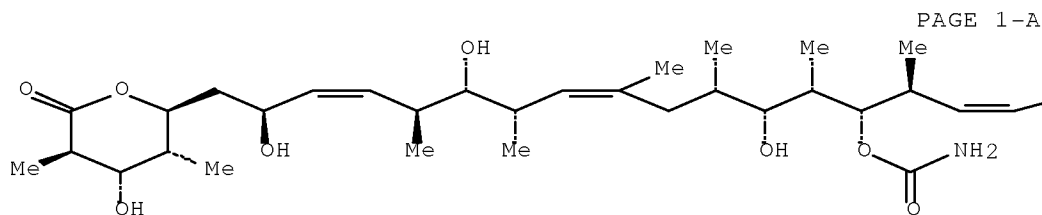
NTE overall yield via iodine substituted pyran-2-one intermediate =
10%

RX(351) OF 354 COMPOSED OF RX(15), RX(16), RX(17), RX(24), RX(25), RX(33),
RX(26), RX(27), RX(11), RX(28), RX(29), RX(30)

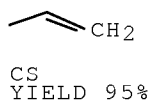
RX(351) BM + BP + BR + 2 L + CI + CE + AV +
CP ==> CS



12
STEPS
➔



PAGE 1-B



RX(15)	RCT	BM 136320-64-4
	PRO	BO 132969-60-9
	NTE	Swern oxidation
RX(16)	RCT	BO 132969-60-9, BP 77877-20-4
	RGT	V 121-44-8 Et ₃ N, F 60669-69-4 F ₃ CSO ₃ BBu ₂
	PRO	BQ 132969-62-1
RX(17)	RCT	BQ 132969-62-1, BR 6638-79-5
	RGT	BT 75-24-1 AlMe ₃
	PRO	BS 252342-49-7
	SOL	109-99-9 THF
	NTE	yield over 5 steps starting from Roche's ester = 72%
RX(24)	RCT	BS 252342-49-7, L 69739-34-0
	STAGE(1)	
	RGT	N 108-48-5 2,6-Lutidine
	STAGE(2)	
	RGT	CG 1333-74-0 H ₂
	CAT	12135-22-7 Pd(OH) ₂
	SOL	64-17-5 EtOH
	STAGE(3)	
	RGT	U 26412-87-3 Pyridine-SO ₃ (1:1), E 7087-68-5 EtN(Pr-i) ₂
	PRO	CF 252342-42-0
RX(25)	RCT	CF 252342-42-0
	STAGE(1)	
	RGT	CK 7550-45-0 TiCl ₄
	SOL	75-09-2 CH ₂ Cl ₂

STAGE(2)
 RCT CI 130043-07-1
 CON -78 deg C

STAGE(3)
 RGT CL 76-05-1 F3CCO2H
 SOL 110-54-3 Hexane
 CON room temperature

PRO CJ 252342-43-1

RX(33) RCT CJ 252342-43-1
 RGT CW 54575-49-4 K Selectride
 PRO CM 256920-77-1
 SOL 109-99-9 THF, 108-88-3 PhMe
 NTE stereoselective, ratio of diastereomers = 9:1

RX(26) RCT CM 256920-77-1, L 69739-34-0

STAGE(1)
 SOL 75-09-2 CH2Cl2

STAGE(2)
 RGT AJ 10028-15-6 Ozone
 SOL 75-09-2 CH2Cl2

STAGE(3)
 RGT BE 603-35-0 PPh3

PRO CN 252342-51-1
 NTE yield over 12 steps starting from Roche's ester = 33%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
 RGT CA 1070-89-9 (Me3Si)2N.Na
 PRO AW 850211-74-4
 CON -78 deg C -> -10 deg C
 NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)
 RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
 SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0 Pentane
 CON SUBSTAGE(1) room temperature -> -78 deg C
 SUBSTAGE(2) -78 deg C
 SUBSTAGE(3) -78 deg C -> room temperature
 SUBSTAGE(4) 1 hour, room temperature

STAGE(2)
 RCT AW 850211-74-4
 RGT BA 534-17-8 Cs2CO3
 CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

PRO AX 633293-75-1
 NTE BBN related byproducts were obtained in 10% yield, Suzuki

coupling

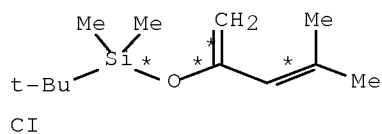
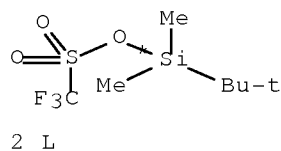
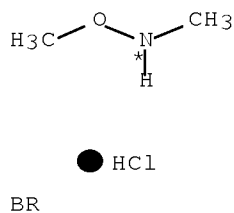
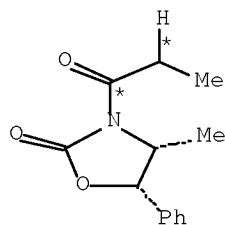
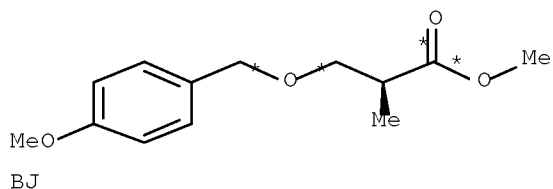
RX(28) RCT AX 633293-75-1
 RGT CC 84-58-2 DDQ
 PRO CO 633293-76-2
 SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
 CON 0 - room temperature deg C

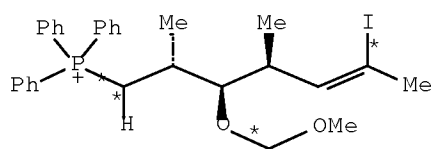
RX(29) RCT CO 633293-76-2, CP 3019-71-4
 RGT CR 1344-28-1 Al₂O₃
 PRO CQ 633293-93-3

RX(30) RCT CQ 633293-93-3
 RGT CT 7647-01-0 HCl
 PRO CS 127943-53-7
 SOL 7732-18-5 Water, 67-56-1 MeOH
 NTE overall yield via iodine substituted pyran-2-one intermediate = 10%

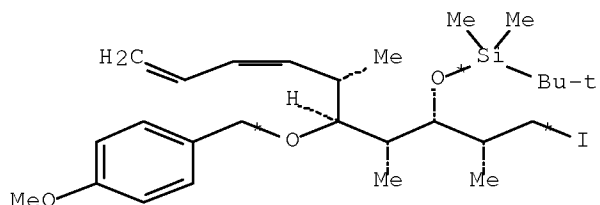
RX(352) OF 354 COMPOSED OF RX(14), RX(15), RX(16), RX(17), RX(24), RX(25),
 RX(33), RX(26), RX(27), RX(11), RX(28), RX(29), RX(30)

RX(352) BJ + BP + BR + 2 L + CI + CE + AV +
 CP ==> CS

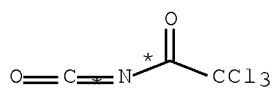




CE

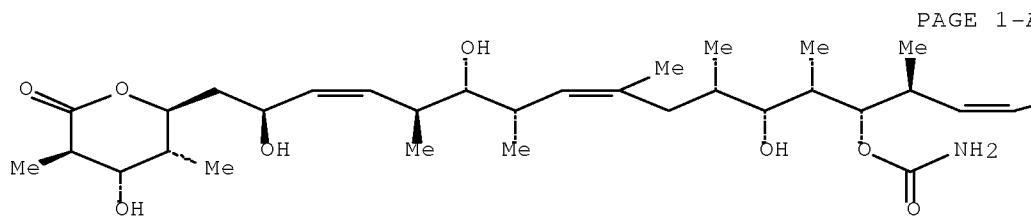


AV



CP

13
STEPS
→



PAGE 1-B



CS
YIELD 95%

RX(14) RCT BJ 132969-71-2
RGT BN 16853-85-3 LiAlH4
PRO BM 136320-64-4
SOL 109-99-9 THF

RX(15) RCT BM 136320-64-4
PRO BO 132969-60-9
NTE Swern oxidation

RX(16) RCT BO 132969-60-9, BP 77877-20-4
 RGT V 121-44-8 Et3N, F 60669-69-4 F3CSO3BBu2
 PRO BQ 132969-62-1

RX(17) RCT BQ 132969-62-1, BR 6638-79-5
 RGT BT 75-24-1 AlMe3
 PRO BS 252342-49-7
 SOL 109-99-9 THF
 NTE yield over 5 steps starting from Roche's ester = 72%

RX(24) RCT BS 252342-49-7, L 69739-34-0

 STAGE(1)
 RGT N 108-48-5 2,6-Lutidine

 STAGE(2)
 RGT CG 1333-74-0 H2
 CAT 12135-22-7 Pd(OH)2
 SOL 64-17-5 EtOH

 STAGE(3)
 RGT U 26412-87-3 Pyridine-SO3 (1:1), E 7087-68-5 EtN(Pr-i)2

 PRO CF 252342-42-0

RX(25) RCT CF 252342-42-0

 STAGE(1)
 RGT CK 7550-45-0 TiCl4
 SOL 75-09-2 CH2Cl2

 STAGE(2)
 RCT CI 130043-07-1
 CON -78 deg C

 STAGE(3)
 RGT CL 76-05-1 F3CCO2H
 SOL 110-54-3 Hexane
 CON room temperature

 PRO CJ 252342-43-1

RX(33) RCT CJ 252342-43-1
 RGT CW 54575-49-4 K Selectride
 PRO CM 256920-77-1
 SOL 109-99-9 THF, 108-88-3 PhMe
 NTE stereoselective, ratio of diastereomers = 9:1

RX(26) RCT CM 256920-77-1, L 69739-34-0

 STAGE(1)
 SOL 75-09-2 CH2Cl2

 STAGE(2)
 RGT AJ 10028-15-6 Ozone
 SOL 75-09-2 CH2Cl2

 STAGE(3)
 RGT BE 603-35-0 PPh3

PRO CN 252342-51-1
 NTE yield over 12 steps starting from Roche's ester = 33%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
 RGT CA 1070-89-9 (Me3Si)2N.Na
 PRO AW 850211-74-4
 CON -78 deg C -> -10 deg C
 NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)
 RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
 SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0 Pentane
 CON SUBSTAGE(1) room temperature -> -78 deg C
 SUBSTAGE(2) -78 deg C
 SUBSTAGE(3) -78 deg C -> room temperature
 SUBSTAGE(4) 1 hour, room temperature

STAGE(2)
 RCT AW 850211-74-4
 RGT BA 534-17-8 Cs2CO3
 CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

PRO AX 633293-75-1
 NTE BBN related byproducts were obtained in 10% yield, Suzuki coupling

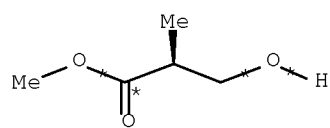
RX(28) RCT AX 633293-75-1
 RGT CC 84-58-2 DDQ
 PRO CO 633293-76-2
 SOL 7732-18-5 Water, 75-09-2 CH2Cl2
 CON 0 - room temperature deg C

RX(29) RCT CO 633293-76-2, CP 3019-71-4
 RGT CR 1344-28-1 Al2O3
 PRO CQ 633293-93-3

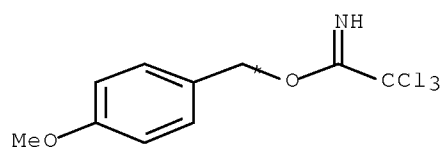
RX(30) RCT CQ 633293-93-3
 RGT CT 7647-01-0 HCl
 PRO CS 127943-53-7
 SOL 7732-18-5 Water, 67-56-1 MeOH
 NTE overall yield via iodine substituted pyran-2-one intermediate = 10%

RX(353) OF 354 COMPOSED OF RX(13), RX(14), RX(15), RX(16), RX(17), RX(24),
 RX(25), RX(33), RX(26), RX(27), RX(11), RX(28), RX(29), RX(30)

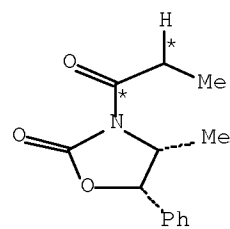
RX(353) BI + AD + BP + BR + 2 L + CI + CE +
 AV + CP ==> CS



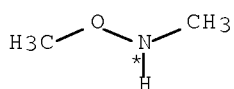
BI



AD



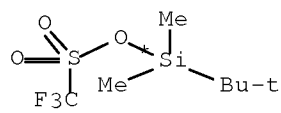
BP



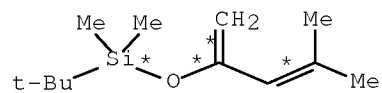
BR



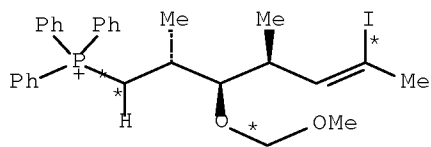
HCl



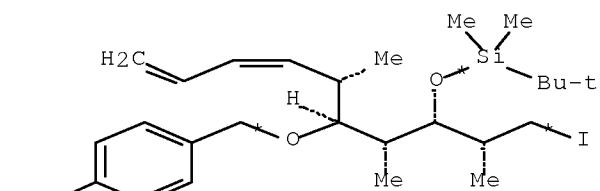
2 L



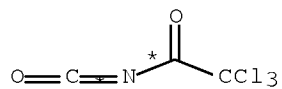
CI



CE

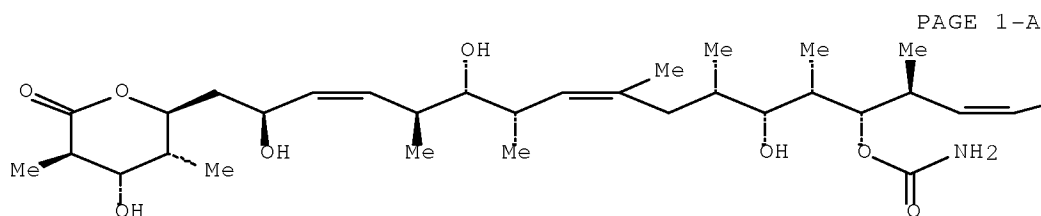


AV

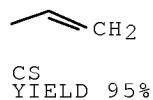


CP

14
STEPS
→



PAGE 1-B



RX(13)	RCT	BI 80657-57-4, AD 89238-99-3
	RGT	BK 24057-28-1 Pyridinium tosylate
	PRO	BJ 132969-71-2
	SOL	75-09-2 CH ₂ Cl ₂ , 110-82-7 Cyclohexane
RX(14)	RCT	BJ 132969-71-2
	RGT	BN 16853-85-3 LiAlH ₄
	PRO	BM 136320-64-4
	SOL	109-99-9 THF
RX(15)	RCT	BM 136320-64-4
	PRO	BO 132969-60-9
	NTE	Swern oxidation
RX(16)	RCT	BO 132969-60-9, BP 77877-20-4
	RGT	V 121-44-8 Et ₃ N, F 60669-69-4 F ₃ CSO ₃ BBu ₂
	PRO	BQ 132969-62-1
RX(17)	RCT	BQ 132969-62-1, BR 6638-79-5
	RGT	BT 75-24-1 AlMe ₃
	PRO	BS 252342-49-7
	SOL	109-99-9 THF
	NTE	yield over 5 steps starting from Roche's ester = 72%
RX(24)	RCT	BS 252342-49-7, L 69739-34-0

STAGE(1)

RGT N 108-48-5 2,6-Lutidine

STAGE(2)
 RGT CG 1333-74-0 H2
 CAT 12135-22-7 Pd(OH)2
 SOL 64-17-5 EtOH

STAGE(3)
 RGT U 26412-87-3 Pyridine-SO3 (1:1), E 7087-68-5 EtN(Pr-i)2

PRO CF 252342-42-0

RX(25) RCT CF 252342-42-0

STAGE(1)
 RGT CK 7550-45-0 TiCl4
 SOL 75-09-2 CH2Cl2

STAGE(2)
 RCT CI 130043-07-1
 CON -78 deg C

STAGE(3)
 RGT CL 76-05-1 F3CCO2H
 SOL 110-54-3 Hexane
 CON room temperature

PRO CJ 252342-43-1

RX(33) RCT CJ 252342-43-1
 RGT CW 54575-49-4 K Selectride
 PRO CM 256920-77-1
 SOL 109-99-9 THF, 108-88-3 PhMe
 NTE stereoselective, ratio of diastereomers = 9:1

RX(26) RCT CM 256920-77-1, L 69739-34-0

STAGE(1)
 SOL 75-09-2 CH2Cl2

STAGE(2)
 RGT AJ 10028-15-6 Ozone
 SOL 75-09-2 CH2Cl2

STAGE(3)
 RGT BE 603-35-0 PPh3

PRO CN 252342-51-1
 NTE yield over 12 steps starting from Roche's ester = 33%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
 RGT CA 1070-89-9 (Me3Si)2N.Na
 PRO AW 850211-74-4
 CON -78 deg C -> -10 deg C
 NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)
 RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi

SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) -78 deg C
SUBSTAGE(3) -78 deg C -> room temperature
SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AW 850211-74-4
RGT BA 534-17-8 Cs2CO3
CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

PRO AX 633293-75-1
NTE BBN related byproducts were obtained in 10% yield, Suzuki
coupling

RX(28) RCT AX 633293-75-1
RGT CC 84-58-2 DDQ
PRO CO 633293-76-2
SOL 7732-18-5 Water, 75-09-2 CH2Cl2
CON 0 - room temperature deg C

RX(29) RCT CO 633293-76-2, CP 3019-71-4
RGT CR 1344-28-1 Al2O3
PRO CQ 633293-93-3

RX(30) RCT CQ 633293-93-3
RGT CT 7647-01-0 HCl
PRO CS 127943-53-7
SOL 7732-18-5 Water, 67-56-1 MeOH
NTE overall yield via iodine substituted pyran-2-one intermediate =
10%

L3 ANSWER 9 OF 9 CASREACT COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 130:38235 CASREACT Full-text
TITLE: Total Synthesis of (+)-Discodermolide
AUTHOR(S): Marshall, James A.; Johns, Brian A.
CORPORATE SOURCE: Department of Chemistry, University of Virginia,
Charlottesville, VA, 22901, USA
SOURCE: Journal of Organic Chemistry (1998), 63(22), 7885-7892
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

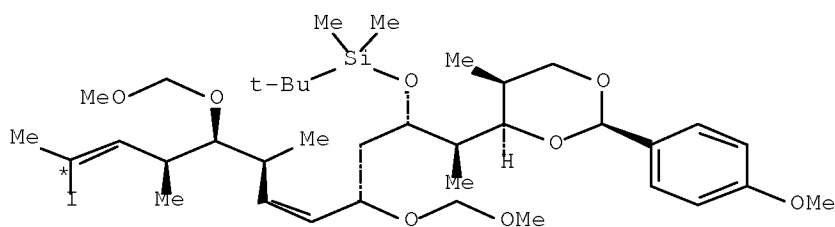
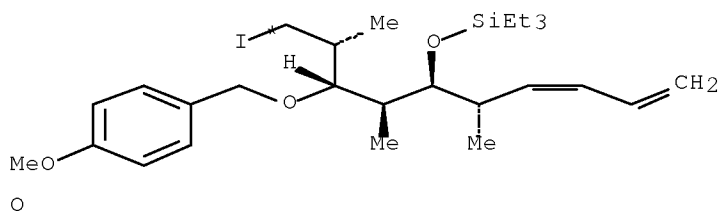
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The total synthesis of (+)-discodermolide (I) is described. The approach involves assemblage of three key stereotriad subunits through addition of nonracemic allenyltin, -indium, and -zinc reagents to (S)-3-silyloxy-2-methylpropanal derivs., followed by reduction of the resulting anti,syn- or

syn,syn-homopropargylic alc. adducts to the (E)-homoallylic alcs. and subsequent Sharpless epoxidn. Addition of Me cuprate reagents or Red-Al to the resultant epoxy alcs. yielded the key precursors, (2S,3S,4S)-HC.tplbond.CCH(α Me)CH(β OCH₂OMe)CH(β Me)CH₂OSiEt₃ (II), aldehyde (III), and (2S,3R,4S,5S,6Z)-HOCH₂CH(α Me)CH(α OCH₂C₆H₄-4-OMe)CH(α Me)CH(α OSiEt₃)CH(β Me)CH=CHCH=CH₂ (IV). Addition of alkyne II (as the lithio species) to aldehyde III afforded the propargylic alc. (V) as the major stereoisomer. Lindlar hydrogenation and installation of appropriate protecting groups led to an aldehyde which was converted to the (Z)-vinylic iodide (VI) upon treatment with α -iodoethylidene triphenylphosphorane. Suzuki coupling of this vinylic iodide with a boranate derived from iodide of IV led to the coupled product (VII) with the complete carbon backbone of (+)-discodermolide and the correct stereochem. The synthesis was completed by cleavage of the cyclic PMP acetal at C1 with i-Bu₂AlH and three-step oxidation-esterification to the ester. Cleavage of the C19 Et₃Si ether and C19 carbamate formation followed by cleavage of the remaining alc. protecting groups, first with DDQ and then aqueous HCl, afforded I.

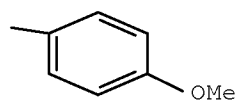
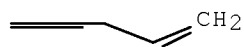
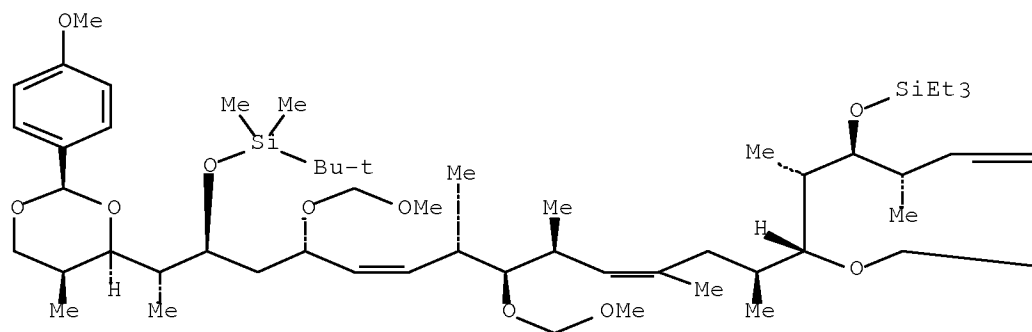
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(5) OF 7 ...O + R ==> S



R

(5) \rightarrow



S
YIELD 74%

RX(5) RCT O 216669-69-1, R 216669-22-6

STAGE (1)

RGT T 594-19-4 t-BuLi

SOL 60-29-7 Et20

STAGE (2)

RGT U 280-64-8 9-BBN

SOL 109-99-9 THF

STAGE (3)

RGT V 7789-78-8 CaH2

CAT 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-

SOL 68-12-2 DMF

PRO S 216669-75-9

=> d his

(FILE 'HOME' ENTERED AT 14:33:15 ON 06 MAY 2009)

FILE 'CASREACT' ENTERED AT 14:33:53 ON 06 MAY 2009

L1 STRUCTURE UPLOADED

L2 0 S SSS L1

L3 9 S SSS L1 FULL

=> s l3 and (ay<2004 or py<2004 or pry<2004)

80910 AY<2004

528110 PY<2004

31094 PRY<2004

L4 2 L3 AND (AY<2004 OR PY<2004 OR PRY<2004)

=> d scan

L4 2 ANSWERS CASREACT COPYRIGHT 2009 ACS on STN

TI Synthesis of discodermolide and variants thereof

RX(11) OF 354 - REACTION DIAGRAM NOT AVAILABLE

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L4 2 ANSWERS CASREACT COPYRIGHT 2009 ACS on STN

TI Total Synthesis of (+)-Discodermolide

RX(5) OF 7 - REACTION DIAGRAM NOT AVAILABLE

ALL ANSWERS HAVE BEEN SCANNED

=> d scan l4 bib ti 1-2

'1-2' IS NOT A VALID FORMAT FOR FILE 'CASREACT'

L4 2 ANSWERS CASREACT COPYRIGHT 2009 ACS on STN

TI Synthesis of discodermolide and variants thereof

RX(11) OF 354 - REACTION DIAGRAM NOT AVAILABLE

The following are valid formats:

ABS ----- GI and AB

ALL ----- BIB, AB, IND, RE, Single-step Reactions

APPS ----- AI, PRAI

BIB ----- AN, plus Bibliographic Data

CAN ----- List of CA abstract numbers without answer numbers

CBIB ----- AN, plus Compressed Bibliographic Data

DALL ----- ALL, delimited (end of each field identified)

IABS ----- ABS, indented with text labels

IALL ----- ALL, indented with text labels

IBIB ----- BIB, indented with text labels

IND ----- Indexing data

IPC ----- International Patent Classifications

ISTD ----- STD, indented with text labels

OBIB ----- AN, plus Bibliographic Data (original)

OIBIB ----- OBIB, indented with text labels

SBIB ----- BIB, no citations
 SIBIB ----- IBIB, no citations

 MAX ----- Same as ALL
 PATS ----- PI, SO
 SCAN ----- TI and FCRD (random display, no answer number. SCAN
 must be entered on the same line as DISPLAY, e.g.,
 D SCAN.)
 SSRX ----- Single-Step Reactions (Map, Diagram, and Summary for
 all single-step reactions)
 STD ----- BIB, IPC, and NCL

 CRD ----- Compact Display of All Hit Reactions
 CRDREF ----- Compact Reaction Display and SO, PY for Reference
 FHIT ----- Reaction Map, Diagram, and Summary for first
 hit reaction
 FHITCBIB --- FHIT, AN plus CBIB
 FCRD ----- First hit in Compact Reaction Display (CRD) format
 FCRDREF ----- First hit in Compact Reaction Display (CRD) format with
 CA reference information (SO, PY). (Default)
 FPATH ----- PATH, plus Reaction Summary for the "long path"
 FSPATH ----- SPATH, plus Reaction Summary for the "short path"
 HIT ----- Reaction Map, Reaction Diagram, and Reaction
 Summary for all hit reactions and fields containing
 hit terms
 OCC ----- All hit fields and the number of occurrences of the
 hit terms in each field. Includes total number of
 HIT, PATH, SPATH reactions. Labels reactions that have
 incomplete verifications.
 PATH ----- Reaction Map and Reaction Diagram for the "long
 path". Displays all hit reactions, except those
 whose steps are totally included within another hit
 reaction which is displayed
 RX ----- Hit Reactions (Map, Diagram, Summary for all hit reactions)
 RXG ----- Hit Reaction Graphics (Map and Diagram for all hit reactions)
 RXL ----- Hit Reaction Long (Map, Diagram, Summary for all hit reactions)
 RXS ----- Hit Reaction Summaries (Map and Summary for all hit reactions)
 SPATH ----- Reaction Map and Reaction Diagram for the "short
 path". Displays all single step reactions which
 contain a hit substance. Also displays those
 multistep reactions that have a hit substance in both
 the first and last steps of the reaction, except for
 those hit reactions whose steps are totally included
 within another hit reaction which is displayed

To display a particular field or fields, enter the display field
 codes. For a list of the display field codes, enter HELP DFIELDS
 at an arrow prompt (=>). Examples of combinations include: D TI;
 D BIB RX; D TI, AU, FCRD. The information is displayed in the same order
 as the specification. All of the formats, except CRD, CRDREF, FHIT, PATH,
 FPATH, SPATH, FSPATH, FCRD, FCRDREF, HIT, RX, RXG, RXS, SCAN, and OCC, may
 be used with the DISPLAY command to display the record for a specified
 Accession Number.

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> d scan 14 bib ti 2
 '2' IS NOT A VALID FORMAT FOR FILE 'CASREACT'

TI Total Synthesis of (+)-Discodermolide

RX(5) OF 7 - REACTION DIAGRAM NOT AVAILABLE

The following are valid formats:

ABS ----- GI and AB
 ALL ----- BIB, AB, IND, RE, Single-step Reactions
 APPS ----- AI, PRAI
 BIB ----- AN, plus Bibliographic Data
 CAN ----- List of CA abstract numbers without answer numbers
 CBIB ----- AN, plus Compressed Bibliographic Data
 DALL ----- ALL, delimited (end of each field identified)
 IABS ----- ABS, indented with text labels
 IALL ----- ALL, indented with text labels
 IBIB ----- BIB, indented with text labels
 IND ----- Indexing data
 IPC ----- International Patent Classifications
 ISTD ----- STD, indented with text labels
 OBIB ----- AN, plus Bibliographic Data (original)
 OIBIB ----- OBIB, indented with text labels

 SBIB ----- BIB, no citations
 SIBIB ----- IBIB, no citations

 MAX ----- Same as ALL
 PATS ----- PI, SO
 SCAN ----- TI and FCRD (random display, no answer number. SCAN
 must be entered on the same line as DISPLAY, e.g.,
 D SCAN.)
 SSRX ----- Single-Step Reactions (Map, Diagram, and Summary for
 all single-step reactions)
 STD ----- BIB, IPC, and NCL

 CRD ----- Compact Display of All Hit Reactions
 CRDREF ----- Compact Reaction Display and SO, PY for Reference
 FHIT ----- Reaction Map, Diagram, and Summary for first
 hit reaction
 FHITCBIB --- FHIT, AN plus CBIB
 FCRD ----- First hit in Compact Reaction Display (CRD) format
 FCRDREF ---- First hit in Compact Reaction Display (CRD) format with
 CA reference information (SO, PY). (Default)
 FPATH ----- PATH, plus Reaction Summary for the "long path"
 FSPATH ----- SPATH, plus Reaction Summary for the "short path"
 HIT ----- Reaction Map, Reaction Diagram, and Reaction
 Summary for all hit reactions and fields containing
 hit terms
 OCC ----- All hit fields and the number of occurrences of the
 hit terms in each field. Includes total number of
 HIT, PATH, SPATH reactions. Labels reactions that have
 incomplete verifications.
 PATH ----- Reaction Map and Reaction Diagram for the "long
 path". Displays all hit reactions, except those
 whose steps are totally included within another hit
 reaction which is displayed
 RX ----- Hit Reactions (Map, Diagram, Summary for all hit reactions)
 RXG ----- Hit Reaction Graphics (Map and Diagram for all hit reactions)

RXL ----- Hit Reaction Long (Map, Diagram, Summary for all hit reactions)
 RXS ----- Hit Reaction Summaries (Map and Summary for all hit reactions)
 SPATH ----- Reaction Map and Reaction Diagram for the "short
 path". Displays all single step reactions which
 contain a hit substance. Also displays those
 multistep reactions that have a hit substance in both
 the first and last steps of the reaction, except for
 those hit reactions whose steps are totally included
 within another hit reaction which is displayed

To display a particular field or fields, enter the display field
 codes. For a list of the display field codes, enter HELP DFIELDS
 at an arrow prompt (=>). Examples of combinations include: D TI;
 D BIB RX; D TI, AU, FCRD. The information is displayed in the same order
 as the specification. All of the formats, except CRD, CRDREF, FHIT, PATH,
 FPATH, SPATH, FSPATH, FCRD, FCRDREF, HIT, RX, RXG, RXS, SCAN, and OCC, may
 be used with the DISPLAY command to display the record for a specified
 Accession Number.

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> d scan l4 bib ti
 INVALID SCAN FIELD FOR FILE 'CASREACT'

One or more of the display fields specified are not valid with DISPLAY
 SCAN in the current file. Enter HELP DSCAN at the arrow prompt (=>)
 for the list of fields that may be used when scanning the answers.

=> d l4 bib ti 1-2

L4 ANSWER 1 OF 2 CASREACT COPYRIGHT 2009 ACS on STN
 AN 142:411149 CASREACT Full-text
 TI Synthesis of discodermolide and variants thereof
 IN Smith, Amos B., III; Freeze, Brian Scott; Xian, Ming
 PA The Trustees of the University of Pennsylvania, USA
 SO PCT Int. Appl., 61 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005035489	A2	20050421	WO 2004-US33473	20041012
	WO 2005035489	A3	20050804		
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RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 20070276144	A1	20071129	US 2007-575136	20070509
PRAI	US 2003-510097P		20031009		
	WO 2004-US33473		20041012		
OS	MARPAT 142:411149				

TI Synthesis of discodermolide and variants thereof

L4 ANSWER 2 OF 2 CASREACT COPYRIGHT 2009 ACS on STN
AN 130:38235 CASREACT Full-text
TI Total Synthesis of (+)-Discodermolide
AU Marshall, James A.; Johns, Brian A.
CS Department of Chemistry, University of Virginia, Charlottesville, VA,
22901, USA
SO Journal of Organic Chemistry (1998), 63(22), 7885-7892
CODEN: JOCEAH; ISSN: 0022-3263
PB American Chemical Society
DT Journal
LA English
TI Total Synthesis of (+)-Discodermolide
RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d l4 bib ti 2

L4 ANSWER 2 OF 2 CASREACT COPYRIGHT 2009 ACS on STN
AN 130:38235 CASREACT Full-text
TI Total Synthesis of (+)-Discodermolide
AU Marshall, James A.; Johns, Brian A.
CS Department of Chemistry, University of Virginia, Charlottesville, VA,
22901, USA
SO Journal of Organic Chemistry (1998), 63(22), 7885-7892
CODEN: JOCEAH; ISSN: 0022-3263
PB American Chemical Society
DT Journal
LA English
TI Total Synthesis of (+)-Discodermolide
RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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COST IN U.S. DOLLARS	SINCE FILE	TOTAL
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FULL ESTIMATED COST	224.05	224.27
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
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PASSWORD:

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SESSION RESUMED IN FILE 'CASREACT' AT 15:08:48 ON 06 MAY 2009
FILE 'CASREACT' ENTERED AT 15:08:48 ON 06 MAY 2009
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COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	224.05	224.27
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-7.02	-7.02

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COST IN U.S. DOLLARS	SINCE FILE	TOTAL
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FULL ESTIMATED COST	224.05	224.27
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-7.02	-7.02

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